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ON  
G A L L - S T O N E S  
OR  
CHOLELITHIASIS



ON

GALL-STONES

OR

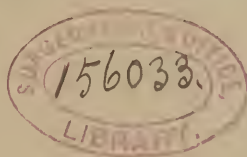
CHOLELITHIASIS

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PHILADELPHIA

P. BLAKISTON, SON & CO.

1012, WALNUT STREET

1896



TO

D. J. LEECH, M.D., D.Sc., F.R.C.P.,

PROFESSOR OF MATERIA MEDICA AND THERAPEUTICS IN THE  
VICTORIA UNIVERSITY,

WHO FIRST SUGGESTED THIS WORK TO ME,

AND TO WHOM

I AM GRATEFUL FOR MUCH KIND

ADVICE IN ITS PROSECUTION.



## PREFACE.

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THE present volume is a continuation of some experiments on the solvent action of various drugs on gall-stones which I carried out in 1892, at The Owens College, Manchester, to provide material for my Dissertation for the Degree of Doctor of Medicine. Since that date my interest has been extended to the ætiology, pathology, and treatment of cholelithiasis, and I have made a few further observations bearing on these aspects of the disease. In referring, during my own investigations, to the experience of other observers, I felt the want in our literature of a work containing an account of the present condition of our knowledge of the disease, and to attempt to fill that vacant place is the object of the present book. I do not claim to set forth much new or original matter now, but rather to give a concise but complete statement of the published observations and opinions of various writers which bear on the elucidation of the nature of a disease which is but imperfectly understood.

In referring to the work of Continental observers I have received much help from the valuable monographs on cholelithiasis by Naunyn and Courvoisier, as the frequent reference in the text to these authors shows. Both these writers are amongst the highest

authorities on the subject, so it has also been necessary to quote their own opinions somewhat freely. Gumprecht's papers ("Neuere Fortschritte in der Kenntniss der Cholelithiasis") in the 'Deutsche medicinische Wochenschrift' for 1895 are very valuable, giving as they do a *résumé* of the most important recent work on the subject of cholelithiasis, and concluding with an extensive bibliography,—chiefly, however, of the Continental literature of the disease. No book on gall-stones would be complete without frequent reference to the writings of Mayo Robson, who has had a large experience and great success in the surgical treatment of the disease and its complications.

I must here acknowledge, and express my thanks to the above writers for, the help which I have received from their works in the production of this book.

I am also very much indebted to Dr. Leech, Dr. Dreschfeld, Dr. Steell, and Dr. Harris, of the Manchester Royal Infirmary, for kind permission to refer to cases of gall-stones which were in hospital under their care whilst I was Resident Medical Officer there, and to my friend Dr. T. A. Goodfellow for his valuable assistance in the monotonous and troublesome work of proof correcting, and for many helpful suggestions made during the printing of the book.

E. M. B.

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# ON GALL-STONES OR CHOLELITHIASIS.

## CHAPTER I.

Definition of the Disease—Anatomy of the Biliary Passages—Varieties of Gall-stones—Facets on Biliary Calculi—Shape of the Concretion—Chemical Constitution of Gall-stones—Seat of Formation of Gall-stones.

### Definition of the Disease.

GALL-STONES, or biliary calculi, or biliary concretions, are masses of varying shape, size, consistency, and constitution, which are formed during life in the bile-ducts of the liver or in the gall-bladder by the conglomeration, amorphous or crystalline, of the precipitated portions of the normal constituents of the bile, some of the precipitated bodies uniting with each other to form new compounds.

The causes which determine this precipitation of the normal constituents of bile from their state of solution have not yet been definitely determined.

The term Cholelithiasis is applied to the pathological conditions of the body which result in the formation of gall-stones; and the symptoms which during life are considered to be manifestations of the presence of calculi in the biliary system are spoken of as “attacks of cholelithiasis” or of “gall-stones.”

### Anatomy of the Biliary Passages.\*

A short account of the anatomy of those portions of the liver concerned in cholelithiasis will be of use in making a description of the disease and its complications more clear.

The disease develops in the excretory apparatus of the liver, which consists of the intra-hepatic ducts, the hepatic duct, the cystic duct, the gall-bladder, and the common bile-duct.

The *intra-hepatic ducts* are the fine radicles of the system of biliary ducts, and they arise around the lobules of the liver.

The *hepatic duct*, formed by the union of a right and left branch which issue from the bottom of the transverse fissure and unite at a very obtuse angle, descends to the right, within the gastro-hepatic omentum, in front of the vena portæ, and with the hepatic artery to its left. Its diameter is about two lines ( $\frac{1}{6}$  inch, 4 mm.), and its length nearly two inches (about 50 mm.). At its lower end it meets with the cystic duct descending from the gall-bladder, and the two ducts unite together at an acute angle to form the common bile-duct.

The *gall-bladder* is a pear-shaped membranous sac 3 or 4 inches (100 mm.) long, about  $1\frac{1}{2}$  inches (40 mm.) across its widest part, and capable of containing 8—12 fluid drachms (30—40 c.cm.). It is lodged obliquely in the fossa under the surface of the right lobe, with its large end or *fundus*, which projects beyond the anterior border of the liver, directed downwards, forwards, and to the right, whilst its *neck* is inclined in the opposite direction. Its upper surface is attached to the liver by areolar tissue. Its under surface and fundus are covered by the peritoneum which is reflected over them from the surface of the liver. In rare cases the peritoneum completely surrounds the gall-bladder, which is then suspended by a sort of mesentery from the under surface of the liver. The fundus touches the abdominal parietes immediately beneath the margin of the thorax opposite the tip of the tenth costal cartilage. The gall-bladder rests below on the

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\* 'Quain's Anatomy,' 9th edition.

commencement of the transverse colon; and, further back, it is in contact with the duodenum, and sometimes with the pyloric extremity of the stomach. The *neck* gradually narrowing is curved like the letter S, and then, becoming more constricted, and changing its general direction altogether, it beads downwards and terminates in the cystic duct.

The gall-bladder is supplied with blood by the cystic artery, a branch of the right division of the hepatic artery, along which vessel it also receives nerves from the celiac plexus. The cystic vein empty themselves into the vena portæ.

The *cystic duct* is  $\frac{1}{12}$  inch (2 mm.) in diameter, and about  $1\frac{1}{2}$  inches (40 mm.) in length. It runs backwards, downwards, and to the left, and unites with the hepatic duct to form the common bile-duct.

The *common bile-duct*, or *ductus communis choledochus*, from two to three lines ( $\frac{1}{4}$  inch, 6 mm.) in width and nearly 3 inches (80 mm.) in length, conveys the bile to the duodenum. It passes downwards and backwards, continuing the course of the hepatic duct, between the layers of the gastro-hepatic omentum in front of the vena portæ, and to the right of the hepatic artery. Passing behind the first part of the duodenum it reaches the descending portion, and continues downwards on the inner and posterior aspect of that part of the intestine, covered by or included in the head of the pancreas, and for a short distance in contact with the right side of the pancreatic duct. Together with that duct it then perforates the muscular wall of the duodenum, and after running obliquely for three quarters of an inch between its coats, and forming an elevation beneath the mucous membrane, it becomes somewhat constricted, and opens by a common orifice with the pancreatic duct on the inner surface of the intestine, near the junction of the second and third portions of the duodenum, and three or four inches beyond the pylorus.

*Varieties of the biliary system met with in man.*—The gall-bladder is occasionally wanting, in which case the hepatic duct is much dilated within the liver or in some part of its course. Sometimes the gall-bladder is irregular in form or is constricted across its middle, or, but much more rarely, it is partially divided in a longitudinal direction. Direct communications by means of small ducts (hepato-cystic), passing from the liver to the gall-bladder, exist regularly in various animals, and they are sometimes found, as an unusual formation, in the human subject. The right and left divisions of the hepatic duct sometimes continue separate for some distance within the gastro-hepatic omentum.

Lastly, the common bile-duct not unfrequently opens separately from the pancreatic duct into the duodenum.

*Structure of the ducts.*—The intra-hepatic ducts have walls of fibrillar connective tissue, within which is a basement membrane and a lining of short columnar epithelium. According to Heidenhain, they also possess both longitudinally and circularly disposed muscular coats in their wall.

In the portal canals, where they are somewhat larger, the ducts present numerous openings on the inner surface, which are scattered irregularly in the larger ducts, but in the subdivisions are arranged in two longitudinal rows, one at each side of the vessel. These openings were formerly supposed to be the orifices of mucous glands; but, while the main ducts are studded with true mucous glands of lobulated form and with minute orifices, the openings now referred to belong to saccular and tubular recesses, which are often branched and anastomosing, and may be beset all over with caecal projections. The larger bile-ducts and the gall-bladder have areolar coats, containing abundant elastic tissue and a certain amount of plain muscular tissue disposed both longitudinally and circularly. They are lined with columnar epithelium.

The *lymphatic vessels* arise between the lobules, unite with larger vessels which run along the portal canals, and emerge at the portal fissure. Other lymphatics accompany the branches of the hepatic veins, and others arise on the surface of the organ beneath the peritoneum, which on the upper surface communicate with the thoracic lymphatics, and on the under surface with the lymphatics of Glisson's capsule.

### Varieties of Gall-stones.

The following classification and description of the different forms of calculi is that adopted by Naunyn.\*

1. *Pure Cholesterin Stones.*—These are firm, yellowish-white, oval, or round calculi, varying in size from that of a cherry to that of a pigeon's egg or even larger. They rarely show any of the brown or greenish coloration which is an indication of the

\* 'Klinik der Cholelithiasis,' 1892.

presence of bile pigments and their compounds. On fracture they are seen to be formed by a radial arrangement of crystals of cholesterin around a centre which is often composed of a brownish matrix. They show no signs of stratification, and the surface is smooth or else roughened by a sprinkling of crystals. Facets are rarely present.

2. *Stratified Cholesterin Stones* are in form and size like pure cholesterin stones, but they vary in colour from yellowish-white to green, brown, or brownish-black. They are generally faceted, and more or less distinctly stratified. The layers are of various thicknesses and colour, and the outer ones are glassy or earthy in texture, whilst those nearer the centre are distinctly crystalline, and do not show so much stratification. The crystals in the centre of the calculus occasionally form a kind of nucleus around which the outer layers are deposited. The central crystals often assume a radial arrangement.

The stones of the first group are composed of pure cholesterin, whilst those of the second variety contain 90 per cent. or more of the same substance. In the clear parts the cholesterin is the purest, but it is also present in large quantity in the coloured layers, where it is mixed with bilirubin-calcium (brown) and biliverdin-calcium (green). Pure calcium carbonate is also met with at times in the green layers.

3. *Common, or Gall-bladder Calculi*.—The majority of gall-stones belong to this group. They are of various colours, and in size range from that of a pin's head up to but rarely exceeding that of a large cherry. They are generally faceted and when fresh are pulpy,

but when removed from the gall-bladder they soon harden and shrivel. They have a stratified structure, with generally a firm shell around a softer pulpy nucleus in which may often be found a central cavity containing a yellowish alkaline fluid. No crystalline formation can be made out by the naked eye in these stones.

4. *Mixed Bilirubin-Calcium Calculi* are found in the gall-bladder or large ducts, either singly or in twos and threes. In the latter case they bear facets, formed by mutual pressure. Their shape varies with their seat of formation, and in size they are very often equal to or greater than that of a cherry.

They are formed of dark thick concentric layers which enclose a small yellowish central nucleus of crystalline cholesterin. The outer dark or reddish-brown layers may also contain as much as 25 per cent. of cholesterin, but their mass is composed of a compound of bilirubin and calcium, with perhaps traces of copper, and iron also in combination with bilirubin.

5. *Pure Bilirubin-Calcium Calculi* are rarely larger than a pea, and are often as small as grains of sand. In character they are either irregular, solid, waxy, blackish-brown masses, or else hard, brittle, nodular, or stalk-shaped spongy structures of a metallic steel-grey or black colour. In the hollow spaces which are contained in the latter variety of concretion some of the small soft stones of the former type are found. Both varieties of this form of calculus consist almost entirely of bilirubin-calcium, with only traces of the other bile pigments or their compounds.

The presence of cholesterin is generally hard to demonstrate, and it may even be absent entirely in this form of gall-stone.

6. *Rarer Forms of Biliary Calculi.*—(a) *Amorphous or Imperfectly Crystallised Cholesterin Gall-stones* are calculi which, as a rule, resemble pearls in outward appearance. They vary in size between that of a grain of sand and that of a large pea, and they contain a dark nucleus of bilirubin-calcium formation. In structure they are imperfectly crystalline, show no stratification, and apart from the central nucleus consist entirely of cholesterin.

(b) *Calcium Carbonate* occurs in many stones, either in the free state or combined with biliary pigments. It rarely, however, as uncombined chalk forms the main constituent of a biliary calculus. Gall-stones containing much chalk are always very hard. Frerichs described a large biliary calculus which was coated with chalk, and calcified conditions of the walls of the gall-bladder are at times met with.

(c) *Concretions containing Foreign Bodies.*—It frequently happens that a calculus which is composed chiefly of cholesterin contains a nucleus of bilirubin-calcium formation, or a crystal of cholesterin may be the starting point and be contained in the centre of a bilirubin-calcium stone. Although a small biliary concretion may act as a nucleus for the growth of a much larger calculus, it rarely happens that a true foreign body is found in the centre of a gall-stone. A few cases of this nature have, however, been recorded, such as a round-worm, a *Distoma hepaticum*,

a plum stone, a needle, a small aggregation of blood, and soft albuminous bile-stained casts of the small intra-hepatic biliary ducts.

Bilirubin-calcium concretions which arise in the hepatic ducts at times pass down through the hepatic duct into the gall-bladder or into the common duct, where they may act as a "foreign" body, around which more stone-forming materials are deposited to form a larger calculus.

(d) *Casts of the Ducts*, though common in cattle, are rare in man. Small brittle bilirubin-calcium stones, which are practically casts of the finer intra-hepatic ducts in which they grow, are at times met with in the *post-mortem* room.

### Facets on Biliary Calculi.

Facets on biliary calculi are formed, in Naunyn's opinion, by mutual pressure, and not by friction between the stones. The latter process may, however, occur, though he has never met with an instance of it. The pressure is exerted on the calculi whilst they are in a soft condition, and a section of a stratified calculus shows a regular arrangement of the various layers with no evidence of their having been ground down by friction. The superficial layers, those which feel the effects of the pressure most, are more compact and, in calculi containing pigment, more deeply coloured than the deeper layers of the same stone.

The edges and corners of calculi may, however, be split off at times by pressure.

### The Shape of a Gall-stone.

The shape of a gall-stone depends in great part on the seat of its development, and on the number present at the same time in their nursery. Calculi, however numerous, taken from the same situation always have the same characteristics of structure and constitution. Single concretions in the gall-bladder may be oval, spherical, or form a complete cast of its interior. In the large extra-hepatic ducts they are oval, spherical, or more cylindrical, and at times they form a cast of a portion of the interior of the duct.

When several stones are present in either the gall-bladder or large ducts, they are subjected to mutual pressure, in consequence of which they lose their spherical or ovoid shape and become polyhedral from the formation on them of flattened surfaces or "facets." A number of these faceted calculi are frequently bound together in the gall-bladder by a pasty material composed of biliary detritus and bile, to form a conglomeration-cast of the interior of the bladder.

Concretions in the smaller ducts sometimes form a cast of the lumen of the tube in which they lie, or else they are of an irregularly spherical or nodular shape. By the conglomeration of several small concretions a horny stalk-like or a mulberry-shaped mass may be formed.

Pure cholesterin calculi not uncommonly lie in a recess in the wall of the larger ducts or gall-bladder, in which case they take the shape of the cavity in which they have developed. The surface of these

latter stones is generally rough from the adhesion to it during life of the surrounding mucous membrane, and large solitary calculi, or those occurring with one or two others, have as a rule a rough surface. Faceted calculi are generally smooth.

### Chemical Constitution of Gall-stones.

Cholesterin and bilirubin-calcium are the most important constituents of biliary calculi. Free calcium carbonate is perhaps the next in order of frequency and importance; and calcium also occurs in combination with biliverdin, and with the less known biliary constituents, bilifuscin, bilicyanin, and bilihumin.

In some calculi small quantities of bilirubin and its pigment derivatives are found in an uncombined state. Fatty acids and soaps form at times an appreciable part of calculi.

Gamgee\* states that neither the bile salts nor free bilirubin ever actually form part of a gall-stone in man, and that when traces of them are found it is because they are important constituents of the bile which permeates calculi at times. Thudichum,† however, quotes the analysis of Neukomm of a human gall-stone which contained a large amount of bile acids and their calcium compounds. Metallic mercury has been found in gall-stones (Budd,‡ Frerichs,§ &c.), and also copper and iron (Budd, Thudichum, &c.). Phosphates

\* 'Physiological Chem. of the Animal Body,' vol. ii, p. 381.

† 'A Treatise on Gall-stones,' 1863.

‡ 'Lectures on Diseases of the Liver,' 3rd edition.

§ 'Klinik der Leberkrankheiten,' vol. ii; New Syd. Soc. transl., vol. xiii.

of calcium and other metals (Charcot\*) occur as rare constituents of gall-bladder calculi, but in those concretions which in escaping from the body have passed through the bowel or urinary passages (Güterbock†) they are present in large quantity. Uric acid is also found on calculi which have escaped through the urinary organs.

Biliary calculi which have remained in the intestine for some time are generally coated with fæcal matter.

For a detailed analysis of the various kinds of gall-stones, reference should be made to the works of Thudichum and Gamgee. The latter author also gives an account of the most recent methods adopted in making such analyses.

### Seat of the Formation of Gall-stones.

Gall-stones may form in any portion of the biliary passages, that is in the fine intra-hepatic branches or in the larger extra-hepatic ducts, the hepatic, cystic, and common bile-ducts, or in the gall-bladder. As a rule they arise and develop in the gall-bladder, but not at all infrequently the common duct and the small radicles of the biliary system are the seats of the origin and development of gall-stones. Calculi in the cystic and common ducts have, however, as a rule worked their way there from the intra-hepatic ducts or especially from the gall-bladder. In the majority of cases the concretions are formed in the lumen of the passage, but at times they arise within

\* 'Leçons sur les Maladies du Foie, &c.,' 1877, p. 133.

† 'Virchow's Archiv,' 1876.

the mucous membrane which lines the wall of the larger biliary passages and gall-bladder. I have met with two cases in which the mucous membrane of the gall-bladder was seen with the naked eye to be dotted with many small dark specks like black grains of sand, which could be easily picked out with a sharp-pointed instrument. Microscopical preparations of the above specimens showed that the black specks were small gall-stones consisting of beautiful clear crystals of cholesterin of the ordinary type collected together in large numbers and covered in places with biliary pigment. In some of the concretions the cholesterin was solidified into more of an amorphous glass-like formation. These small cholesterin gall-stones were lying in spaces in the mucous membrane which looked like "retention-cysts." I described and figured these "intra-mucous" gall-stones in the 'Manchester Medical Chronicle' for December, 1893, and January, 1894. Large concretions also lie at times in a saccular outgrowth from the wall of the gall-bladder or of the common duct. They consist for the most part of cholesterin.

Calculi which are found in the gall-bladder may have started their life in the intra-hepatic bile-ducts, whence they work their way down through the hepatic and cystic ducts whilst they remain of small size. In the gall-bladder they increase in size by the deposition on them of stone-forming material.

In rare cases the gall-bladder is found to be like a honeycombed structure with no distinct central cavity. The septa of the network are formed of tissue which is really an outgrowth from the mucous mem-

brane of the original wall, and in each of the spaces thus formed a gall-stone is found. A very good specimen of this nature is preserved in the pathological museum at the Owens College, Manchester. The above condition is probably an exaggeration of that in which the small black particles described above occur.

## CHAPTER II.

Physiology and Chemistry of Cholesterin—Physiology and Chemistry of the Bile Salts—The solvent capacity of the Bile Salts for Cholesterin—Decomposition of the Bile Salts—Physiology and Chemistry of the Bile Pigments—The Calcium of the Bile—The Fats and Soaps of the Bile—The total daily quantity of Bile—The secretion pressure of Bile.

Physiology and Chemistry of Cholesterin.

CHOLESTERIN occurs normally in many of the tissues of the body. It is most abundant in all nervous tissue, especially in the white substance: large numbers of its crystals form in the spirit in which specimens of brains are kept. The corpuscles of the blood contain .25 per cent., and the plasma and serum from .02 to .06 per cent. of cholesterin (Hoppe-Seyler\*), and it is present in the testis, ovary, and lens of the eye. Of the normal secretions and excretions of the body it occurs in solution in milk, semen, bile, mucus from mucous membranes, and in the crystalline form in the fæces.

Pathologically, cholesterin is met with in many conditions, generally in association with fluids, and it then almost invariably appears in its crystalline form. It is seen at times in sputum from bronchiectatic and phthisical cavities, hydatid cysts, especially

\* 'Physiologische Chemie,' 1877, p. 401.

when suppuration has set in, collections of pus, pyonephrosis, empyemata, &c., ovarian, dermoid, thyroid, and brain cysts, the vitreous chamber of the eye, &c. &c. It is also met with in atheromatous ulcers and cholesteatomata and other tumours.

It is, however, as a constant constituent of the bile of man that cholesterol is most important. The quantity present in healthy human bile varies. Cope-  
man and Winston\* found .099 gram., Mayo Robson† .045 gram., Noël Paton and Balfour‡ .062 gram., of cholesterol in 100 c.c. of bile obtained from healthy women by means of a biliary fistula. In bladder bile Frerichs§ found 1.18 per cent., and Hoppe-Seyler|| .35 per cent.

The much larger amount which is found in bladder bile as compared with fistula bile is probably due to concentration of the former by absorption of water through the mucous membrane of the gall-bladder.

An abnormally large amount of cholesterol is frequently present in the bile as the result of certain pathological processes which develop in many people, especially when they are above fifty years of age. As a result of this increase in the quantity of cholesterol in the bile, gall-stones develop.

Cholesterol ( $C_{26}H_{43}OH$ ) is a monatomic alcohol which occurs in a crystalline form. From anhydrous ether or chloroform it crystallises in the form of needles which contain no water, and from alcohol or ether containing water it separates in the form of

\* 'Journ. Physiol.,' vol. x.

† 'Proc. Roy. Soc.,' vol. xlvii.

‡ 'Laboratory Reports Roy. Coll. Phys. Ed.,' 1891.

§ Op. cit.

|| Op. cit., p 301.

rhombic plates with a corner chipped out. The latter form is the well-known typical cholesterin crystal. The individual crystals are colourless, but when many are seen together they appear to be white. Cholesterin is insoluble in water, solutions of inorganic compounds and glycerin, but it is readily soluble in alcohol, ether, chloroform, turpentine, amyl and ethyl nitrite, paraldehyde, acetone, &c. &c., fats, soaps, and solutions of the bile salts.

Cholesterin is held in solution in the bile by the three last substances. The effect of a solution of animal soap in distilled water on a crystal of cholesterin is very remarkable and characteristic. It is best seen under the microscope, by allowing a drop of a .5 per cent. solution to run in under the cover-glass to a crystal of cholesterin. The crystal becomes at once covered with minute clear colourless outgrowths, which rapidly increase in size and appear like intestinal villi in shape. These villous-like processes enlarge very rapidly, and finally become detached from the parent mass and float freely in the surrounding soap solution. What was originally a typical solid crystal of cholesterin is eventually changed into many of these new bodies which are of a viscous nature. These viscous soap-cholesterin formations assume chiefly a spherical shape, which appears to be made up of several globules of different sizes, arranged in the form of a nest inside a large outer spherical covering. If the bodies be placed in water they swell up, become clearer and less viscid in appearance, until a certain stage is reached in which the soap solution in them seems to be too

weak to retain the cholesterin, which is then deposited in a crystalline form again. This short description of the soap-cholesterin bodies is important in connection with similar forms which appear in human bile at times, and which are supposed to play an important part in the formation of biliary calculi.

I published a longer account of the above action which I found that soap had on cholesterin, in the 'Manchester Medical Chronicle,' December, 1893, and January, 1894, and also in my 'Graduation Dissertation' in 1893.

We are chiefly concerned in this place with considering the appearance of cholesterin in human bile, a subject the study of which is, however, rendered rather difficult by the fact that very little is definitely known concerning the physiological processes which determine its presence there.

There are three processes, any one or all of which may be responsible for the appearance of cholesterin in normal bile. They are—

1. The liver may excrete cholesterin from the blood where it exists pre-formed as a result of the metabolism of certain of the tissues of the body, especially of the nervous system.

2. Cholesterin may be formed and excreted by the bile as a result of hepatic metabolism itself.

3. The mucous membrane lining the bile-ducts and gall-bladder may secrete cholesterin and pour it out into the bile.

1. The first of the above processes has, up to recent times at any rate, been generally considered to be the one responsible for the appearance of chole-

terin in human bile, although no strong evidence could be advanced in support of the supposition.

Gamgee\* thinks that, normally, the liver acts "in reference to cholesterol purely as an excretory organ." In support of this opinion he refers to Austin Flint's statement that the blood of the jugular vein invariably contains much more cholesterol than that of the carotid artery; and also to the assertions of Frerichs, Becquerel, and Rodier, that in cases of jaundice with complete obstruction to the flow of bile into the intestine the amount of cholesterol in the bile is remarkably increased. Gamgee admits, however, that it is in the highest degree advisable that these particular determinations should be repeated with accurate modern, instead of the cruder earlier, methods.

On the other hand, Jankau† found that no increased excretion of cholesterol in the bile took place after its administration in solution to animals by the mouth and by subcutaneous injection; and, further, that the quantity of cholesterol present in the bile was quite unaffected by variations in the diet of the animal. In Gamgee's opinion, however, these experiments were too crude and obviously fallacious, and the conclusions from them are much less trustworthy than those based on the observations of Frerichs, namely, that the arrest of the excretion of bile certainly is followed by an increase of cholesterol in the blood above the normal amount.

\* Op. cit., p. 339.

† 'Archiv f. exper. Path. u. Pharm.,' vol. xxxix. Ref. Naunyn, op. cit., p. 10.

2. There is no direct evidence either for or against the theory that cholesterin is formed as a result of hepatic metabolism, and its improbability can best be arrived at by a process of exclusion. The cholesterin in the normal bile is much more likely to be produced by the action of either or both of the other possible processes. Were cholesterin formed by the metabolism of the liver substance, one would expect to find more of it present in the bile of an animal with a very large liver, such as an ox, than there actually is the case. Thudichum\* even states that cholesterin does not occur in ox bile, but I have extracted it myself, though in but slight amount.

3. The remaining explanation of the presence of cholesterin in normal bile—namely, that it arises from the mucous membrane which lines the biliary passages—is one which has received a great deal of attention of late, and which is gaining more and more supporters every day.

Budd,† as early as 1845, considered that the cholesterin of gall-stones was probably dependent upon, and formed by, the coats of the gall-bladder when in a state of fatty degeneration. Bristowe,‡ in 1887, from the facts of the case mentioned a little later in this chapter, was led to assume, and was almost inclined to think, that the bulk of the cholesterin in gall-stones formed in the gall-bladder is derived, not from bile, but from secretions discharged from the mucous surface of the organ.

\* 'Med. Press and Cir.,' Nov. 16th, 1892.

† Op. cit.

‡ 'Lancet,' Feb. 19th, 1887.

The most prominent advocate in recent times of the formation of cholesterin normally by the mucous membrane of the bile passages is Naunyn.\* He supports his belief, in the first place, by the results of the experiments mentioned previously, in which Jankau administered cholesterin in solution to animals in their food, and found that it did not appear in increased quantity in the bile. (Gamgee† thinks that Naunyn is not justified in arriving at such a conclusion from the experiments performed.) In the second place, Naunyn‡ states that cholesterin is contained in the secretions of other mucous membranes besides that of the biliary passages. He has found it in the sputum of catarrhal bronchitis to the extent of ·09 per cent., and in that of fœtid bronchitis (·15 per cent.). I have myself frequently found cholesterin in the mucus which one coughs up from the lungs in health. This latter observation can easily be verified by allowing a little of the mucus which is coughed up in the morning to dry slowly on a watch glass, and then examining the dried residue with a low power of the microscope. I am also inclined to think that cholesterin occurs in the secretion of those mucous membranes which have more of a protective (*e. g.* those lining the bile-ducts, bronchi, &c.) than a secretive (stomach, &c.) function.

Pathology, by emphasising physiological processes, frequently throws light on obscure points which experimental research has quite failed to elucidate. In the point under consideration this is specially noticeable.

\* *Op. cit.*

† *Op. cit.*, p. 340.

‡ *Op. cit.*, p. 13.

I have frequently examined bile obtained *post mortem* from the gall-bladders of patients who have generally been in or beyond the prime of life, and who have died from cardiac or various other chronic diseases, without there being any evidence of cholelithiasis either in life or after death. When taken out of the gall-bladder the bile will be found to be full of columnar epithelium cells desquamated from the mucous membrane of the ducts, either singly or in clusters. Mixed with these cells may be found a few cholesterolin crystals, &c. In the course of a few days the cells begin to disappear and crystals of cholesterolin to appear in great numbers, until finally no traces of the cells can be found, but the fluid is full of cholesterolin crystals in innumerable profusion.

Again, with the cystic duct completely obstructed or obliterated, so that the access of bile to the gall-bladder is impossible, the latter is often found to contain fluid without any traces of bile in it, and which to the naked eye is seen to sparkle with crystals of cholesterolin, and calculi in such a sealed-up gall-bladder show evidence of growth from the deposition of pure cholesterolin on them.

In one case of chronic Bright's disease I found a single stone the size of a large marble firmly gripped by the wall of the gall-bladder about midway between the fundus and neck, and completely shutting off the cavity in the fundus from all communication with the cystic duct. On the cystic duct side of the calculus was ordinary bile, whilst the space between the stone and the fundus of the gall-bladder contained yellowish fluid in which a large number of spark-

ling crystals of cholesterin were seen with the naked eye.

Finally, large gall-stones are at times found developing in a sacculated outgrowth of the wall of the biliary passage, and in two cases I saw embedded in the mucous membrane of the gall-bladder many small black specks, which on being examined microscopically were found to consist of cholesterin in a crystalline form lying apparently in retention-cysts.

Bristowe\* recorded a case in which crystals of cholesterin in masses one eighth by one sixth of an inch in size were found embedded in cavities in the thickened wall of a gall-bladder in which the cystic duct had been obliterated for some time. The cavities appeared to Bristowe to be evidently dilated mucous crypts.

It must, however, be acknowledged that, in cases of obstruction of the cystic duct, all the gall-bladder may contain a large quantity of a clear mucus-like fluid in which no cholesterin can be found.

I think that from the above facts it is not unreasonable to conclude that cholesterin is formed by the mucous membrane of the biliary passages under certain pathological conditions, the nature of which cannot be definitely stated. The cholesterin may be formed as a result of degeneration of the cell elements of the mucous membrane, but it is also possible that some of the glands which exist in profusion in the wall of the biliary passages may secrete it.

To Gamgee the formation of cholesterin seems to be a result of the degeneration of cell protoplasm,

\* 'Lancet,' Feb. 19th, 1887.

especially where this is accompanied by the appearance of fatty matters.

Taking all the above physiological and pathological evidence into consideration, it is very probable that under normal conditions the greater part of the cholesterin which is found in bile is derived from the mucous membrane of the biliary passages, but that a portion of it is excreted by the liver from the blood, in which it exists already as a product of the metabolism of the tissues of the body, especially of the nervous system.

### Physiology and Chemistry of the Bile Salts.

The bile salts are the sodium compounds of glycocholic acid  $\left\{ \begin{array}{c} \text{C}_{24}\text{H}_{40}\text{O}_5 \\ \text{C}_2\text{H}_5\text{NO}_2 \end{array} \right\}$  and taurocholic acid  $\left\{ \begin{array}{c} \text{C}_{24}\text{H}_{40}\text{O}_5 \\ \text{C}_2\text{H}_7\text{NO}_3\text{S} \end{array} \right\}$ . Both have a common basis of cholalic acid, with which glycine and taurine combine separately to form their respective acids.

*Cholalic acid*,  $\text{C}_{24}\text{H}_{40}\text{O}_5$ , is a non-nitrogenous crystalline compound, which is sparingly soluble in cold water, but more readily in boiling water. It is not present in fresh bile, but it is found in decomposed bile and in the contents of the large and small intestines. Its presence in the intestines is accounted for by the supposition that part of the bile salts is there split up into cholalic acid and glycine and taurine. Cholalic acid is supposed to be formed by the liver cells, though nothing definitely is known concerning its formation nor of its forerunners. Where it unites with the glycine and taurine is also uncertain, but pro-

bably the liver is the organ which is responsible for their combination. It gives the colour reaction of the bile salts with Pettenkofer's test.

*Glycin*, *glycocine*,  $C_2H_5NO_2$ , is a crystalline compound containing nitrogen. It is readily soluble in water, and is formed as the result of the pancreatic digestion of nitrogenous foods, and when gelatin is subjected to the digestive action of trypsin (Gangee\*). It is increased by a vegetable diet, and when injected or introduced into the body is reduced to, and excreted as, urea by the kidneys (Halliburton†). When it is heated with urea outside the body, uric acid is formed. Glycin is more abundantly met with in herbivorous animals and in man than in the carnivorous animals, in which it only occurs in small amounts.

*Taurin*,  $C_2H_7NO_3S$ , is a crystalline body containing nitrogen and sulphur. It is less soluble in water than glycin is. Taurin is formed as a result of the decomposition of proteids (Gangee‡), and probably by the pancreatic digestion of nitrogenous foods containing sulphur. It is most abundant in carnivorous animals, only small amounts occurring in man and in the herbivora.

The whole of the sulphur contained in the bile is probably derived from the taurin, as all the other organic constituents of the bile are sulphur-free.

*The bile acids appear in the bile in combination with sodium*, and not in the free state.

*Glycocholate of soda* occurs in the bile of the herbi-

\* Op. cit., p. 348.

† 'Text-book of Chemical Physiology and Pathology,' 1891, p. 776.

‡ Op. cit., p. 348.

vora, forming by far the greater portion of the bile salts present. It never occurs in the bile of carnivorous animals (Gamgee\*). The quantity present in human bile occupies a position between these two extremes, and varies greatly according to different authorities, and probably at different times in the same person.

*Taurocholate of soda* is the only bile salt present in the bile of the carnivora, whilst in herbivorous animals it occurs in but very small quantity. In man it is generally present in varying amount, but almost always in less quantity than the glycocholate of soda.

The following table compiled from Gamgee† and Hoppe-Seyler‡ shows the quantities of both salts found in normal human bile by different authorities. The first five results were derived from bile which was obtained during life from cases of biliary fistula, and the last two from bile taken from the gall-bladder after death. The quantities of the salts are expressed in the number of grammes of them extracted from 100 c.c. of fresh bile.

	Jacobsen.	Yeo and Herroun.	Copenau and Winston.	Mayo Robson.	Paton and Balfour.	Hoppe- Seyler.	Socoloff.
Glycocholate of soda .	1·01	·165	} ·628	·751	·356§	3·03	4·8
Taurocholate of soda .	0·0	·055		·009	·049§	·87	1·56

\* Op. cit., p. 294.

† Op. cit., p. 346.

‡ Op. cit., p. 300.

§ The acids are given here.

Mayo Robson's\* and Paton and Balfour's† cases are the most recent, and their patients enjoyed good health in spite of their biliary fistulæ.

It will be seen that the bladder bile contains much more of both salts than does fistula bile. This fact is thought to be due in part to a process of concentration of the bile through absorption of its water, which takes place whilst the bile remains in the gall-bladder. It is also supposed that some of the bile salts which escape into the intestine with the normal expulsion of bile are re-absorbed, carried to the liver, and excreted by that organ, passing into the bile again. At any rate Stadelmann‡ found that four days after the formation of a biliary fistula in a dog, the amount of bile salts in the bile which escaped externally was only 25 per cent. of that present on the day of the operation.

If glycocholate of soda be given by the mouth to a dog it will appear in quantity in the bile, which previously contained only a very small amount.

The taurocholate of soda in a dog's bile increases with a nitrogenous (flesh) diet and diminishes when pure carbohydrates are substituted, as the following figures taken from Spiro's§ tables show.

Nature of diet.	Amount of taurocholate of soda in bile in twenty-four hours.
Fasting . . . . .	·95 grm.
250 grm. flesh . . . . .	1·6 „
1000 „ „ . . . . .	2·67 „
200 grm. carbohydrates . . . . .	1·18 „

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\* 'Proc. Roy. Soc.,' vol. xlvii, 1890.

† 'Lab. Reports, Roy. Coll. Phys. Ed.,' 1891.

‡ Ref. Gumprecht, 'Deut. med. Woch.,' 1895, No. 14.

§ 'Du Bois Reymond's Archiv,' 1880, Supp., p. 50.

The taurocholate of soda which, from the above table, is seen to be present in the bile when the animal is being starved and when fed on carbohydrates only, is probably derived from the products of the wasting of the animal's tissues which is constantly going on. These bodies, which result from the normal tissue metabolism, are of a nitrogenous composition, and they are probably formed more abundantly when nitrogen is withheld from the animal's food, for in the latter condition they are used partly as food to support the vital functions until death ensues, or a supply of proper nitrogenous food be given by the mouth.

Hoppe-Seyler\* states that the solids of the bile are present in greater quantity when the animal is fed on flesh than when fed on bread, and that the bile becomes more watery when food is withdrawn.

Noël Paton and Balfour† found, from observations upon a woman with a biliary fistula, that the amount of solids in the bile rose with the amount of nitrogen in the urine. When the latter was excreted at the rate of 5 to 6 grms. in twenty-four hours, the bile solids during the same period amounted to 5.5 grms.; whilst, when the excretion of nitrogen rose to 11 or 12 grms. in twenty-four hours, the bile solids increased to 7.3 grms. When the patient was on a low diet after operation, the amount of bile solids was only .6 gm. in twenty-four hours. No details of the diet are given in this valuable paper, but the nitrogenous output by the kidneys is an indication of the

\* Op. cit., p. 309.

† Loc. cit.

amount of proteid and albuminoid food digested and absorbed into the circulation.

No observations, as far as I know, have been made on the variations in the amount of glycocholate of soda in the bile under different diets, but of course Paton and Balfour's work covers this ground to a certain extent.

It is more than probable, then, that with an increased consumption of nitrogenous foods there is an increased formation of bile salts.

The presence of the bile salts may be recognised by "Pettenkofer's reaction." The test is performed by adding a few drops of a 10 per cent. solution of cane sugar in water to the solution to be tested, which must previously have any albuminous matter contained in it removed. The mixture is then shaken up in a test-tube, and strong sulphuric acid must be added carefully drop by drop, so as not to raise the temperature of the solution above 70° C. If the temperature be allowed to exceed this point the sugar becomes carbonised and hides the true reaction, namely the development, if any bile salts be present, of a deep violet coloration at the junction of the sulphuric acid and the solution which is being tested. This violet coloration is due to the action of the sulphuric acid on the cholalic acid contained in the bile salts, and not to the glycin or taurin.

The above points suggest an explanation of the varying quantities of the two salts which are met with in the different groups of animals. In carnivores the taurocholate of soda preponderates almost

to the exclusion of the glycocholate of soda, and Gamgee even states that the latter does not occur at all in the bile of dogs. The food of carnivorous animals consists almost entirely of sulphur-containing nitrogenous bodies, whilst the herbivora live on sulphur-free nitrogenous food for the greater part, and in the bile of these latter animals glycocholate of soda takes the place of that occupied by taurocholate of soda in the bile of the carnivores. In man the relative amounts and the total quantity of the two salts in the bile vary greatly according to different observations, a fact which is not at all improbably due to the varying amounts of sulphur-containing and sulphur-free nitrogenous, and of non-nitrogenous foods, taken just before and during the observations. The sulphur in the foods goes towards the formation of the taurocholate of soda.

### **The Solvent Capacity of the Bile Salts for Cholesterin.**

This varies according to different authorities. Hoppe-Seyler\* states that a 12 per cent. solution of mixed bile salts will dissolve ·23 grm. of cholesterin, and Naunyn† that a 2·5 per cent. solution will dissolve ·17 grm. of cholesterin at the body temperature.

In some experiments which I carried out recently I found that a 10 per cent. solution of bile salts obtained from ox bile would absorb ·128 grm. of cholesterin, and that a 5 per cent. solution would dissolve ·053 grm. at the body temperature. On cooling such a solution some of the cholesterin will separate out in the crystalline form. I also made some observa-

\* Op. cit., p. 322.

† Op. cit., p. 16.

tions on the relative solvent capacity for cholesterin of glycocholate and of taurocholate of soda, each in solution by itself, and I found that there was practically no difference between the quantity of cholesterin taken up by the two solutions. The cholalic acid or the cholalate of soda is probably that portion of the bile salt which dissolves the cholesterin.

### **Decomposition of the Bile Acids.**

A decomposition of the bile acids or of the bile salts into cholalic acid and glycin and taurin is supposed to take place in the intestines in man, though the process by which this happens is not known. At any rate cholalic acid is found in the fæces in an uncombined condition, but not so glycin and taurin. The bile acids are very insoluble in cold water, and they cannot dissolve cholesterin, at any rate when they are in watery solution. They are very readily formed from the bile salts by acidifying a solution of these substances in water. If the solution be clear, the addition to it of a drop or two of a mineral acid, or of acetic acid, will cause a milky opalescence to appear which is due to the precipitation of the bile acids. This opalescence can be seen when the solution of the bile salts is only of a .05 per cent. strength. If a solution of bile salts in water, which is naturally alkaline in reaction, containing cholesterin dissolved in it, be but slightly acidified, the bile salts are changed into bile acids, and as a result the latter, being almost insoluble in water, are precipitated. In consequence of the transformation of the soluble bile salts into insoluble bile acids, there remains

nothing in solution in the water to prevent the cholesterin from separating out, and it is therefore precipitated.

A decomposition of the bile salts is supposed by some writers to take place in the biliary system, and to cause a precipitation of cholesterin which they have been holding in solution. As a result of such a precipitation the cholesterin collects together in the crystalline form, and a gall-stone originates, which increases in size by subsequent repetitions of the process. It is certain that the cholesterin held in solution in the bile by the bile salts would be precipitated in the biliary passages were the bile salts changed into bile acids there. But it has never been shown, and it is very improbable, that this simple acidification of the bile ever takes place during life in the bile-ducts or gall-bladder. It is much more improbable that the more complicated process of decomposition of the bile salts into cholalic acid and glycin and taurin can happen during life in the bile-ducts if the simpler process does not. To break up a bile acid into its constituents experimentally, it is necessary to boil it with some caustic alkali or mineral acid. It is probable that a decomposition of bile acids takes place in the intestine during life as a normal event, but no facts are known which in any way prove that cholalic acid and glycin and taurin can be liberated from their combinations whilst they remain in the biliary passages during life.

Micro-organisms are supposed to exert such an action on the bile salts in the ducts during life, but here again theory is unsupported by facts.

In the present state of our knowledge on the subject the change from a bile salt to its corresponding acid, or the decomposition of bile acids which are supposed to take place during life in the biliary passages, and which lead to a precipitation of the cholesterin held in solution by the bile salts, are points which must be considered to be not proven.

### Physiology and Chemistry of the Bile Pigments.

*Bilirubin*,  $C_{32}H_{36}N_4O_6$ , is the pigment contained in the normal yellowish or reddish-yellow bile of man and the carnivorous animals.

It occurs in both amorphous and crystalline forms. It is insoluble in water, but is soluble in chloroform, in dilute solutions of sodium and potassium hydrate, and ammonia. It is held in solution in the normal bile by the alkaline bile salts.

Bilirubin forms compounds with bases. The most important of these as affecting man is the calcium compound, which is insoluble in water, chloroform, &c. Bile contains both lime and bilirubin, but normally these bodies do not readily combine, even in very concentrated bile, provided that decomposition be avoided. The addition of lime-water or a solution of calcium chloride to bile will not cause a precipitation of the bilirubin-calcium compound, unless more than an equal volume be added, or unless the bile contain an unusual amount of bilirubin.

The presence of bile salts tends to prevent the combination of the bilirubin and calcium.

Egg albumen and probably albuminous inflammatory secretions facilitate the formation and precipita-

tion of the lime-pigment compound (Naunyn\*). Bilirubin-calcium is a frequent constituent of human gall-stones. When a solution of bilirubin is acted on by nitric acid containing nitrous acid, a play of green, blue, and orange-red colours is seen where the two liquids mix (Gmelin's reaction).

*Biliverdin*,  $C_{32}H_{36}N_4O_8$ , is the green pigment which appears in the normal bile of herbivorous animals. It also occurs in man, and is found not infrequently in the *post-mortem* room. It is probably formed when the bile has remained for an unusually long time in the biliary passages, and is met with when a gall-bladder which has been distended for a lengthened period of time, is opened in life during an operation.

Biliverdin is a product of the oxidation of bilirubin, a process which takes place on exposure of the former to the air. It resembles bilirubin in its physical properties, and forms a compound with calcium similar to that which bilirubin forms.

The green tint seen in Gmelin's reaction, obtained by adding nitric and nitrous acids to a solution of bilirubin, is due to the formation, by oxidation of the latter pigment, of biliverdin; and the blue and orange-red tints, which develop from the green, are the results of the further oxidation of biliverdin into bilicyanin and choletelin respectively, both of which are imperfectly understood biliary pigment derivatives (Gamgeet†).

*Bilihumin* is probably a mixture of two or three derivatives of bilirubin. It does not exhibit Gmelin's

\* Op. cit., p. 19.

† Op. cit., p. 320.

reaction (Gamgee\*). It probably occurs largely in calculi which not uncommonly form in the small intra-hepatic branches of the bile-ducts. Not much is known about the rarer biliary pigment derivatives which are stated to occur in some biliary calculi.

Bilirubin is probably derived from blood-colouring matter, and is formed in the liver (Gamgee\*).

### The Calcium of the Bile.

As calcium compounds play an important part in the formation of calculi, it is thought by some authorities that their occurrence in increased quantity in the food or drinking-water would cause their excretion in an increased amount in the bile. People who live in limestone districts where the drinking-water contains an unusual amount of lime are supposed by many to be especially liable to suffer from gall-stones. Jankau† made some observations on dogs bearing on this point. He gave the animal large amounts of calcium carbonate and neutral calcium phosphate in its food, but was unable to find any corresponding increase in the amount present in the bile after such administration. The greater part of the calcium salts probably passes into the bile in the secretion of the mucous membrane lining the ducts.

### The Fats and Soaps of the Bile.

Fats and soaps appear normally as margarin, stearin, and palmitin, or their compounds, in the bile. The quantity present varies in different sub-

\* Loc. cit.

† Loc. cit.

jects, but it is always greater when the diet contains fat than when it consists of nitrogenous foods only.

In 100 c.c. of bile obtained from biliary fistulæ in women, Jacobsen\* found .15 per cent., Mayo Robson\* .1 per cent., and Noël Paton and Balfour\* .02 per cent. of fats and soaps estimated together. Hoppe-Seyler† extracted 2.1 per cent. of the same from bladder bile.

Jankau‡ found in a dog with a biliary fistula that the quantity of fats and soaps in the bile increased from 1.47 per cent. of the solid residue obtained from evaporating the bile, when the animal was fed on meat, to 4.89 per cent. when fed on fat and bread, and to 6 per cent. when fed on olive oil.

Fats and soaps are both good solvents of cholesterolin; 100 c.c. of oil will dissolve 5 grms. of cholesterolin, and a 2.5 per cent. solution of animal soap will dissolve .9 gm. of the same substance (Happel).§

The effect of a 2.5 per cent. solution of *sapo animalis*|| in distilled water on a gall-stone containing cholesterolin is curious. After standing for a few hours in the solution maintained at the body temperature, the stone becomes coated with a bluish-white filmy covering, which develops into club-shaped excrescences at the corners or angles of the stone. Gentle agitation of the fluid will dislodge the excrescences. On microscopic examination this new material is found to consist of the soap-cholesterin compound described before as resulting from the

\* Loc. cit.

† Op. cit., p. 801.

‡ Loc. cit.

§ Naunyn, op. cit., p. 16.

|| Brockbank, 'Man. Med. Chron.,' Dec., 1893.

action of a solution of soap on a crystal of cholesterin. Under the action of the soap the stone is gradually eroded. In one experiment which I made, a stone lost 34 per cent. of its weight in three weeks. Soaps containing lime will not act in this way on a gall-stone. A gall-stone placed in pure oleic acid kept at the body heat is rapidly dissolved. In one case I found that a mixed cholesterin stone lost 63 per cent. of its weight in two days in oleic acid, and one placed in olive oil lost 68 per cent. of its weight in ten days. If the action of oil or oleic acid on cholesterin be observed under the microscope, it will be seen that both bodies really dissolve the cholesterin, a crystal of the latter vanishing rapidly when acted on by either. The action of the soap, on the other hand, can hardly be described as a true solution of cholesterin, but at any rate a solid becomes a viscous body during the process.

#### **The Total Quantity of Bile Secreted per diem.**

The quantity of bile secreted daily varies according to different authorities. The most recent researches on this subject are those of Mayo Robson, and Noël Paton and Balfour, which have been referred to previously.

Gamgee\* sums up the various results as follows. "We may conclude that the amount of bile secreted by the healthy human subject (when reabsorption of bile from the intestine cannot take place) varies between a pint, and a pint and a half, and the solids between three and a half and four drachms per day."

\* Op. cit., p. 276.

The more fluid taken into the system, the more watery does the bile become.

Spiro\* found that when he gave a dog 80 c.c. of water in the twenty-four hours, 27·6 c.c. of bile escaped through the fistula, but when he increased it up to 1516 c.c., then the quantity of bile increased to 132 c.c.

The bile of women is supposed to be more watery and to contain more fat than that of men.

### **The Secretion-pressure of Bile.**

The secretion-pressure of bile is very low (24 mm. mercury, Noël Paton and Balfour), but it is higher than the blood-pressure in the portal vein in the ratio of 2·45 to 1 (Gamble).†

\* Loc. cit.

† Op. cit., p. 287.

## CHAPTER III.

Comparative Pathology of Cholelithiasis—Geographical Distribution of the Disease—Frequency of the Occurrence of Cholelithiasis in Europe—Causes which Predispose to the Onset of Cholelithiasis: Age, Sex, Pregnancy, Tight Clothing and other conditions which impede the Emptying of the Gall-bladder and Ducts, The Dependent Position of the Fundus of a Normal Gall-bladder, Want of Exercise, Locality—Prevalence of the Disease in Insane People—Enteric Fever as a Cause of Cholelithiasis—Heart Disease and Gout in Cholelithiasis—Cancer of the Biliary Passages as a Cause or Result of the Disease—Arterial Sclerosis, Atheroma, and Urinary Calculi in Cholelithiasis—Is Cholelithiasis a Constitutional Disease?

**Comparative Pathology of Cholelithiasis.**

BEFORE entering on the question of the appearance of gall-stones in man, it will be interesting to state briefly what is known concerning the comparative pathology of the disease.

Thudichum\* states that he could not find any recorded instance of a gall-stone having been found in any of the wild carnivora, and a few inquiries which I made myself from comparative anatomists confirm this. He states, however, that one or two cases have been described in which small concretions were found in the gall-bladders of domesticated carnivores.

I can also find no mention of biliary calculi occurring in wild herbivora. The concretions which are found

\* 'A Treatise on Gall-stones,' Lond., 1863.

in antelopes and goats in Persia and the East, and known as "Bezoars," occur in the alimentary canal, and are probably formed there, and not in the biliary passages.

In domesticated animals gall-stones are met with, but not at all commonly.

To get as accurate information as possible on the subject, I communicated with many of the professors of veterinary science at the various colleges of the United Kingdom, as well as with other veterinary surgeons of large experience. Most of them agree as to the distribution of the disease in the various domestic animals, and also as to the rarity of its occurrence. The following is a summary of the experience of the observers as stated in their letters to me.

*Horses.*—There is no gall-bladder in the liver of the horse, but the blind end of the common duct acts as a rudimentary one. Here, calculi are not uncommonly found which closely resemble in appearance those obtained from man, being faceted and packed together. They generally occur in old horses and ponies.

*Cattle and sheep* have gall-bladders, and concretions occur in them, but not as commonly apparently as in horses, possibly owing to the fact that the latter live generally to a much greater age than butchers' animals are allowed to. In the gall-bladder of oxen round calculi occasionally occur which are composed chiefly of pigment compounds. Concretions occasionally form around the liver-flukes (*Distoma hepaticum*) in the bile passages, and the presence of this

parasite may set up thickening or calcification of the wall of the ducts. I once found some small cinder-like masses about the size of a mustard-seed in the bladder of an ox which were composed of pigment and an amorphous, glassy, brittle material (probably cholesterin) binding together some eggs of the *Distoma*. The butcher from whom I obtained this specimen told me that he not uncommonly found such "cinder"-like masses in the gall-bladders of oxen.

I could obtain no confirmatory evidence of Glisson's statement, quoted by Frerichs,\* that calculi tend to form in the biliary passages of stalled oxen in the winter, and that they are voided by the bowel when the beasts get back to the green food of the pastures in spring. Relying on this statement of Glisson's, the older physicians used to administer green grass in various forms to the subjects (human) of the disease.

*Dogs*.—Biliary concretions are found occasionally in dogs, but generally in animals which have been pet or lap dogs—obese pug dogs, for instance.

*Pigs* are also very occasionally the subjects of gall-stones.

I was unable to obtain any information as to the composition of any of the above-mentioned calculi.

### Geographical Distribution of the Disease.

What is known of the geographical distribution of cholelithiasis is interesting. The disease is rare in India. Morehead† met with it very seldom, and can

\* Op. cit., vol. ii, p. 511.

† 'Researches on Disease in India,' vol. ii, p. 153.

only recollect three or four cases which, to his knowledge, occurred there.

Hirsch\* states that it is not met with in Martinique, Madagascar (nor probably in any tropical countries). It is rare in Egypt, and when it occurs there it is almost invariably in Europeans and Turks and not in the natives.

Bollinger says that it not infrequently occurs in Turkey.

In Europe, cholelithiasis is met with in varying frequency in the different countries. It is not at all common in Italy, and, according to Poulsen's and Peters' statistics (see below) it is much rarer in Denmark than in England and the central portions of the Continent. Harley,† from the number of specimens of gall-stones which he saw in the museums in St. Petersburg and Moscow, considers that the disease is common there. It is also common in France, especially in old people (in 25 per cent. of the patients, mostly old women, of La Salpêtrière Hospital), and in the southern portion of Germany, in Austria, and in Switzerland.

### Frequency of the occurrence of the Disease in Europe.

Cholelithiasis or gall-stones is a very common affection in parts of Europe, but the frequency with which it occurs seems to vary in the different countries. Several observers have recently investigated the subject by tabulating the number of times evidence

\* 'Handbook of Geographical and Historical Pathology.' New Syd. Soc. trans., vol. cxvii, p. 417.

† 'Diseases of the Liver,' 1883, p. 579.

of the disease has been met with in the *post-mortem* examination of subjects of all ages and of various conditions of life who have died from any cause during recent years.

The following table gives a good idea of the extent to which the disease prevails on the Continent and in England. The number of cases in which cholelithiasis occurred is expressed as a percentage of the total number of *post-mortem* examinations used for the purpose of the statistics.

Poulsen*	Copenhagen	1870—1890	3·8 per cent.
Peters†	Kiel		5 „
Munk‡	Munich	1883—1886	5·1 „
Rother†	Munich	1881—1882	6·4 „
Fiedler‡	Dresden		7 „
Schloth†	Erlangen	1862—1886	7·3 „
Hiller†	Munich	1887—1890	7·5 „
Frank‡	Vienna		10 „
Roth†	Basle	1872—1890	10·9 „
Schröder‡	Strassburg	7 years	12·25 „
Brockbank§	Manchester	1891—1895	6·6 „

Hiller's observations were made on subjects above fifteen years of age. The others were made on patients of all ages.

It will be concluded from the above figures that the frequency of the disease varies greatly in different towns of Europe. This is probably so, but at the same time a source of fallacy must be pointed out which may, in part, account for the smallness of some of the numbers, namely, that the gall-bladder is very

\* Ref. 'Centralbl. f. Chir.,' 1893.

† Ref. Gumprecht, 'Deut. med. Woch.,' 1895, No. 14.

‡ Ref. Naunyn, *op. cit.*, p. 36.

§ Published for the first time.

apt to be overlooked in making *post-mortem* examinations, as being a structure of secondary importance, unless the observer be directing special attention to the pathology of this organ. For this reason it is hardly safe to use any records of *post-mortem* examinations for the purpose of estimating the frequency of cholelithiasis unless they have been made under the personal observation of the investigator.

The average of all the above percentages equals 7·5 per cent.

The statistics published by Schröder\* are very complete and accurate, being drawn up from v. Recklinghausen's observations, which are made with great thoroughness.

During four and a half years ending December, 1895, a careful examination of the gall-bladder was made at my request in all the *post-mortems* at the Manchester Royal Infirmary: 742 cases were examined in this way, and in 49 gall-stones were found (6·6 per cent.). The patients of the Infirmary are drawn from the lower middle and labouring classes. Paupers and children under six years of age are, as a rule, not admitted, and the number of patients over sixty taken into the hospital is relatively small.

### Causes which Predispose to the Onset of Cholelithiasis.

The disease is much more common in women than in men, and in old people than in those below adult life.

*Age of the Subjects of Cholelithiasis.*—The tendency to the formation of gall-stones is much more marked

\* Strassburg Doct. Diss., Ref. Naunyn, op. cit.

above thirty years of age than below, and it increases with each succeeding year of life. The following tables show the frequency of the disease in the various decades of life. The first table is based on my observations at Manchester, and the second is that published by Schröder (see Naunyn \*).

TABLE I.—*Manchester Post-mortems.*

Age.	Total No. of <i>Post-mortems.</i>	No. of cases in which gall- stones were found.	Percentage.
0—20 . . .	67 . . . . .	2 . . . . .	2·9
21—30 . . .	112 . . . . .	6 . . . . .	5·3
31—40 . . .	180 . . . . .	6 . . . . .	3·3
41—50 . . .	189 . . . . .	14 . . . . .	7·4
51—60 . . .	128 . . . . .	12 . . . . .	9·3
61 and over . .	66 . . . . .	9 . . . . .	13·6
Total . .	742 . . . . .	49	

TABLE II.—*Schröder.*

0—20 . . .	82 . . . . .	2 . . . . .	2·4
21—30 . . .	188 . . . . .	6 . . . . .	3·2
31—40 . . .	209 . . . . .	24 . . . . .	11·5
41—50 . . .	252 . . . . .	28 . . . . .	11·1
51—60 . . .	161 . . . . .	16 . . . . .	9·9
61 and over . .	258 . . . . .	65 . . . . .	25·2
Total . .	1150 . . . . .	141	

It will be seen that gall-stones are rare in subjects under thirty years of age. Below the age of puberty they are very uncommon, and only a few cases have been recorded. When they are found in early life it is generally in association with some chronic disease, often heart disease. In all the eight cases which I met with in subjects under thirty there was a gross cardiac lesion—mitral stenosis in five, pericarditis in two, and

\* Op. cit., p. 37 et seq.

alcoholic dilatation in the remaining one. Thorowgood\* saw a gall-stone escape from an abscess in the groin of a girl aged ten.

Schröder found biliary calculi present in 25 per cent. of all his subjects above sixty, but I only met with them in 13·6 per cent. of the same class of cases. Charcot† and Cruveilhier, from observations made on aged workhouse people, agree with Schröder's higher percentage. Perhaps it would be found in England also that the disease is more common than my figures indicate, were *post-mortems* made more often on the very old people who die in workhouses.

*Sex.*—The relative liability of males and females to the disease is as follows :—

Sex.	Manchester.	Schröder.
Males .	2·9% of all <i>post-mortems</i> .	4·4% of all <i>post-mortems</i> .
Females	13·3     „     „     .	20·6     „     „

The disease, then, is four or five times as common in women as in men. There are certain reasons why this should be so. Anything which tends to cause obstruction to the outflow of bile from the gall-bladder and biliary passages will predispose to the formation of calculi. Of such causes the following are the most important.

1. *Pregnancy.*—Ninety per cent. of the women in whose bodies Schröder found gall-stones had borne children, but not more than 71 per cent. of my cases had. Pregnancy acts probably by limiting the movements of the diaphragm, and consequently of the liver, during respiration; such movements of the liver pro-

\* 'Path. Soc. Trans.,' 1877, p. 131.

† 'Leçons sur les Maladies du Foie et des Voies Biliaires,' 1877.

mote the expulsion of bile. The movements of the abdominal muscles, which act in the same way, are also restricted. Again, pregnancy induces a patulous condition of the abdominal walls, and allows of a displacement downwards of the liver, which results in the depression of the fundus of the gall-bladder and stretching of the bile-ducts.

2. *Corset-wearing* is a cause which very often predisposes to the formation of gall-stones. The constriction of the waist which is produced by the wearing of this article is transmitted through the lower ribs to the liver, and causes the formation of a groove on the right lobe of this organ, depresses the liver itself as a whole, and makes the longitudinal axis of the gall-bladder assume a more perpendicular direction than is normal. Schröder found gall-stones present *post-mortem* in 59·5 per cent. of all cases of “corset liver” examined, and he also found a “corset liver” in 24·5 per cent. of all the cases of gall-stones which he investigated. Schloth found the latter association of the two conditions in 10·5 per cent., and Rother in 40 per cent., of the cases of gall-stones examined by them. I found a “corset liver” in 17 per cent. of my own female cases. In addition to corsets, any tight clothing which restricts the movements of the abdominal muscles also predisposes to the onset of the disease.

3. *Any conditions which impede the emptying of the gall-bladder*, and thereby induce biliary stagnation, are liable to excite the development of gall-stones. Moveable or floating liver (Weisker\*); adhesions of

\* ‘Schmidt’s Jahrb.’ 1888, p. 249.

the gall-bladder to neighbouring parts (chronic local peritonitis around a duodenal ulcer was present in one of my cases, and in another the gall-bladder was involved and fixed by a general abdominal lymphosarcoma, and in a third by cancer of the ascending colon); constipation with collection of fæces in the hepatic flexure of the colon—are some of the conditions which may act in this way both in women and in men.

The connection between a floating or moveable right kidney and obstruction to the outflow of bile from a gall-bladder has been emphasised by Weisker, and also quite recently by Morris.\* The last-mentioned writer points out that both conditions are induced by tight-lacing, that 80 per cent. of cases of floating kidney appear in females, and that the right kidney is affected thirteen times as often as the left kidney.

A moveable kidney tends to cause distension of the gall-bladder by dragging upon the duodenum and the bile-ducts, thus obstructing the passage of the bile (Morris).

*The dependent position of the fundus of a normal gall-bladder* is an ever-present cause which predisposes to the retention of bile in this organ. If a normal gall-bladder and liver be examined—and this is best done on a model of a frozen normal liver such as is used for teaching purposes—it will be seen that the fundus of the bladder is at a distinctly lower level than that at which the junction of the cystic and hepatic ducts lies. The gall-bladder being directly opposed to the under surface of the right lobe of the

\* 'Brit. Med. Journ.,' Feb. 2, 1895.

liver, follows the direction taken by the anterior margin of the lobe as it curves down to the costal arch. The fundus of the gall-bladder is moveable, and is always the most dependent part of the organ, whilst the cystic duct is higher up, and generally fixed at the hilus of the liver. A line drawn through the long axis of the gall-bladder, passing through the cystic duct at its junction with the hepatic duct, and through the fundus of the organ, will be found to be oblique, running forwards and downwards. The difference of level at the two extremities of such a line is about one inch, when the normal gall-bladder is in a state of medium distension. In the *post-mortem* room the above-mentioned dependent position of the fundus of the gall-bladder can readily be made out, and very frequently it is much exaggerated, especially when the organ is distended with bile.

Any causes which depress the anterior portion of the right lobe of the liver cause at the same time a lowering of the fundus of the gall-bladder. Corset-wearing is the most prominent example of such a cause.

The gall-bladder, therefore, even under normal conditions, has to be emptied against the action of gravity, so that there is a tendency to an incomplete evacuation of its contents, especially if any semi-solid or solid matters be present in it. This dependent position of the fundus of the gall-bladder is much more marked in quadrupeds, where the long axis becomes almost perpendicular.

In man the "leaning forward" posture adopted at

the writing-table tends to bring the gall-bladder more towards the quadruped position, and to increase the difficulty in emptying it, and an easy-chair position acts in the opposite direction.

One of the reasons why literary men frequently suffer from gall-stones may perhaps be found in the position generally occupied by them during their work.

*Exercise.*—There can be no doubt that the want of exercise predisposes to the onset of the disease. The contraction of the abdominal muscles and the movements of the body generally, aid in the expulsion of the bile from the gall-bladder and bile-ducts, so people who lead inactive and sedentary lives are more liable to a sluggish condition of the bile than those who take a good deal of exercise. The want of exercise also tells indirectly on the inactive, and especially on those who are large eaters and who live well generally, by inducing hepatic derangements which may lead to the onset of cholelithiasis.

*Locality.*—Many writers consider that gall-stones are more common in certain localities of the same country than in others, and in explanation thereof state that the use of drinking-water which contains much lime is very likely to predispose to the formation of biliary calculi.

On the other hand, other writers oppose this theory by denying that biliary calculi are more prevalent in districts where the drinking-water is hard than in those where it is soft.

From Jankau's observations, quoted by Naunyn,\*

\* Loc. cit.

it will be seen that the increase of lime salts in the diet of an animal is not followed by an increase in the quantity excreted by the liver.

In all probability drinking-water has very little to do with the causation of gall-stones.

But if biliary calculi are equally prevalent all over certain countries, they are by no means equally common in different nations which live under different conditions of environment.

In the natives of India the disease is very rare, and even in Italy it is by no means common. In Denmark, according to Poulsen's statistics, evidences of cholelithiasis were found in only 3·8 per cent. of 9172 autopsies on adults, whilst in Strassburg in Alsace 12·5 per cent. of the people are subject to the disease. Manchester comes between the two with 6·6 per cent.

Schröder's Strassburg statistics and my own are accurate, the biliary system having been examined specially in all the *post-mortems*, so it is evident that cholelithiasis is more common in Strassburg than it is in Manchester. It is also probable that Poulsen's observations are quite reliable, for the disease seems to be clinically not at all common in Denmark. Thus out of 347 cases in which cholelithiasis was found by *post-mortem* examination, only 32 showed symptoms of it during life. Poulsen's observations were made on adults, a fact which ought to make his average higher than if subjects of all ages were included, as was the case in Schröder's and my own observations.

The reasons for the prevalence of the disease in certain countries of Europe more than in others are

hard to determine in the present condition of our knowledge of the pathological causes of cholelithiasis. I am inclined to think, however, that the various eating and drinking customs adopted by the different nations play an important part in some way or other in the ætiology of the disease. To believe this is one thing, but to prove it is quite another matter. For, although the dietetic customs of two nations who do not suffer to the same extent from gall-stones may be very similar, there is the individual element to consider, and many people in a country may adopt quite a different habit of eating and drinking from that followed by the nation as a whole, and whereas the national diet may not predispose to gall-stones, that of individuals may easily do so.

It can hardly be that the temperature of the various climates in the different countries has any effect on the ætiology of gall-stones, for England is warmer than Denmark and not so mild as Italy, and yet biliary calculi are more prevalent with us than in either of the other two countries.

The causes which we have dealt with so far as predisposing to the formation of gall-stones may be said to act whilst the subjects remain healthy or almost so. But cholelithiasis is also associated with the presence of certain diseases in man, the consideration of which must be entered on before an attempt to define the radical causes of the affection is made.

**Prevalence of Cholelithiasis in Insane Patients.**—Gall-stones occur very commonly in inmates of lunatic asylums, but their presence during life is not usually

suspected. The most recent observations on this point are tabulated here, the results being derived from *post-mortem* examination only.

Observer.	No. of cases examined.		No. of cases in which gall-stones were found.		Percentage.	
	Males.	Females.	Males.	Females.	Males.	Females.
Beadles*	—	50	—	18	—	36%
Snell†	500	500	—	—	9·2%	19·4%
Warnock‡	26	16	3	8	11%	50%
Goodall§	1400		143	141	20%	

Beadles states that lunatics are especially liable to catarrhal affections which may implicate the gall-bladder equally as readily as any other mucous membrane.

In all of Warnock's cases of gall-stones, with one exception, marked heart disease was present. The average age of the eight women was 58 years. In only two of the eleven cases was the disease suspected during life.

**Enteric Fever** is considered by some observers to be not uncommonly an exciting cause of cholelithiasis. Dufort || states that cholecystitis of a simple, phlegmonous or gangrenous nature is not an infrequent complication of enteric fever. Hagenmüller¶ collected 18 such cases which had been recorded in medical literature up to 1876, and Bernheim\*\* in 1889

\* 'Journ. Ment. Sci.,' July, 1892.

† 'Brit. Med. Journ.,' Aug. 12th, 1893.

‡ 'Med. Times and Hosp. Gaz.,' Oct. 13th, 1894.

§ 'Journ. Ment. Sci.,' July, 1892.

|| 'Rev. de Méd.,' 1893, p. 274.

¶ 'Thèse de Paris,' 1876.

\*\* Ref. Dufort, loc. cit., p. 282.

noticed the occurrence of first attacks of biliary colic in cases of typhoid fever. Dufort obtained a history of a previous attack of the same fever in 19 cases of cholelithiasis. In 12 of these 19 cases the first attack of biliary colic came on in less than six months after the subsidence of the fever—twice in the second month, six times in the third, three times in the fourth, and once in the fifth month. All these patients had suffered from a severe form of enteric fever. Five of the 19 cases could hardly, in Dufort's opinion, be attributed to the enteric fever, as the symptoms of cholelithiasis did not come on until ten months or more after the patient had recovered from the fever.

The cause of enteric cholecystitis is probably a micro-organism. Chiari\* found the typhoid bacillus in the contents of the gall-bladder in 19 out of 22 cases of enteric fever, and other observers have also obtained the same bacillus under similar conditions.

Dufort thinks that the *Bacterium coli commune*, or a pyogenic streptococcus, may also cause the inflammation of the gall-bladder in enteric fever. It is doubtful whether the infective organisms enter the biliary passages from the duodenum or through the blood of the portal vein.

Rupture of the gall-bladder may take place through an ulcer in its wall during typhoid fever. An interesting case of this nature may be briefly mentioned here.

Monier-Williams and Sheild† record the case of a

\* 'Prag. med. Woch.,' 1893.

† 'Lancet,' March 2nd, 1895.

woman, aged 31, who was suddenly seized with severe abdominal pain after suffering from what was considered to be typhoid fever for forty-four days. Symptoms of local peritonitis developed to the right of, and above the umbilicus. Laparotomy was performed, and much recent lymph was found under the liver and around the gall-bladder. The latter organ was deeply inflamed, thickened, and adherent, not much enlarged but tightly distended. Low down near the neck of the gall-bladder was a sharply circular, sloughy ulcer the size of a threepenny-piece. There was a slight perforation in the floor of the ulcer through which fluid could escape. The gall-bladder was opened, and some thick offensive pus not mixed with bile escaped. No calculus could be found. The patient made a good recovery.

**Heart Disease and Cholelithiasis**—I have frequently noticed the presence of biliary calculi in the gall-bladders of patients who have died from cardiac disease, and am of the opinion that the passive hyperæmia or venous congestion, which commonly comes on in severe heart lesions, may act as an exciting cause of the formation of an increased amount of cholesterin by the mucous membrane of the gall-bladder and biliary passages. The blood from the former organ enters the portal vein, and so the wall of the bladder will participate in the results of portal obstruction. Why the mucous membrane of the gall-bladder should, when in a state of venous congestion, tend to form more cholesterin than it does normally, I cannot say, unless it be that the partial asphyxiation to which the cells are subjected causes them to

degenerate more profusely but slowly, and during this slow degeneration cholesterin is formed.

The morbid condition of the liver resulting from the venous congestion of chronic heart disease may also lead to the imperfect formation of the bile salts (see p. 85), with a consequent crystallisation of cholesterin owing to a lack of sufficient media for its solution.

The urine of patients suffering from heart disease which leads to hepatic congestion, contains a large amount of urates, and gall-stones or, at any rate, crystals of cholesterin are very commonly found in the gall-bladder in the same patients.

Out of the 49 cases of gall-stones which I have seen, 27 of the patients—which number includes all the cases below thirty years of age—suffered from some gross cardiac lesion, and 6 others from atheroma. The commonest lesion of the heart was mitral stenosis.

The liver is often in a pathological condition when gall-stones are found in its biliary passages. Of my cases of gall-stones it was fatty in 5, congested in 13, “nutmeg” in 11, cirrhotic in 4, and in 6 it showed a corset groove. The liver was apparently normal in only 4 instances.

*Gout* frequently is associated with cholelithiasis, and many authorities consider that there is probably a distinct connection between the two affections (Murchison,\* Harley,† Trousseau,‡ &c.).

\* ‘Clinical Lectures on Diseases of the Liver’ (3rd edit.), p. 632.

† ‘Diseases of the Liver,’ 1883, p. 587.

‡ ‘Clinical Lectures’ (Syd. Soc. ed.), vol. iv, p. 231.

Sénac\* found hereditary or acquired gout present in 95 out of 166 cases of gall-stones. The urine at any rate frequently contains a large quantity of urates in cholelithiasis. The relation between the two affections may possibly be due to a pathological condition of the liver in which the normal processes by which urea and the bile salts are produced are deranged, with the result that urates, and a quantity of bile salts insufficient to dissolve all the cholesterol, are formed.

**Cancer of the Biliary Passages and Cholelithiasis.**—It has been known for many years (Budd,† 1845, and before) that cancer of the biliary passages and liver is frequently associated with the presence of biliary calculi. Yet authorities have differed as to which is the primary disease. Budd, Frerichs,‡ and the older writers considered that the presence of carcinomatous growths in the walls of the biliary passages resulted in a narrowing of their lumen, and a consequent obstruction to the outflow of bile. This obstruction to the escape of bile acts as an exciting cause of the formation of biliary calculi. It has been pointed out, however, that cancer is frequently present along with biliary calculi without there being any evidence of obstruction to the flow of bile (Marchand§), and also that the new growth frequently starts in ulcers and cicatrices resulting from injuries to the walls of the

\* Ref. Gumprecht, 'Deut. med. Woch.,' 1895, No. 14.

† 'Diseases of the Liver,' 3rd edit., London.

‡ Op. cit.

§ Ref. Gumprecht, loc. cit.

ducts from calculi (Heitler,\* Zenker†). Another important point is that the cancerous symptoms are not uncommonly preceded by definite symptoms of gall-stones.

Musser,‡ in a paper compiled chiefly from cases published up to 1889, shows the results of the *post-mortem* examination of 100 cases of primary cancer of the gall-bladder. Gall-stones are recorded as present in only 69 instances. Their absence is stated definitely in three cases. He acknowledges that their absence at the *post-mortem* examination does not prove that they were not present during life. The conclusion he comes to is that gall-stones are only a possible exciting cause of cancer of the gall-bladder and bile-ducts in persons predisposed to cancer.

Statistics published by recent observers bring almost conclusive evidence in favour of the view that cholelithiasis is the cause, and not the result, of cancer of the gall-bladder and bile-ducts.

Courvoisier§ found gall-stones present in 74 out of 84 cases of primary cancer of the gall-bladder; Brodowski§ in 40 out of 40 such cases; Jayle|| (from French literature) in 23 out of 30 cases; Bertrand¶ in 14 out of 15 cases. Siegert,\*\* from cases in his own experience and from those published by other

\* 'Wien. med. Woch.,' 1883.

† 'Deutsch. Arch. f. klin. Med.,' 1889.

‡ 'Trans. Assoc. Amer. Physic.,' 1889.

§ Ref. Naunyn, op. cit., p. 153.

|| 'Société Anat.,' 1893.

¶ Ref. Gumprecht, loc. cit., No. 14.

\*\* 'Pflug. Arch.,' vol. cxxii, p. 353.

writers, comes to the conclusion that gall-stones are at all events a cause of cancer of the gall-bladder and not a consequence of it, and that they occur in 95 per cent. of cases of primary carcinoma of this organ, but only in about 15 or 16 per cent. of secondary carcinoma of the gall-bladder.

According to Schröder,\* 14 per cent. of all cases of gall-stones suffer at the same time from cancer of the biliary passages.

Naunyn† is of the opinion that half the cases diagnosed as cholelithiasis associated with chronic jaundice are either complicated with cancer of the ducts, or are due to this latter disease alone.

The most recent paper on the subject of primary carcinoma of the bile-ducts is by Rolleston.‡ Gall-stones occurred in only 4 out of 11 such cases collected by him. He thinks that calculi are less commonly associated with cancer of the bile-ducts than with cancer of the gall-bladder, but he recognises the possibility of the escape of the stones before the death of the patient, or before the growth has developed to any great extent.

The fact that gall-stones are not so commonly met with in primary carcinoma of the bile-ducts points to the conclusion that calculi are not formed simply as a result of stagnation of bile due to obstruction set up by the growth. Stagnation is much more marked in bile-duct carcinoma, and yet calculi are less common in it than they are in gall-bladder carcinoma.

\* Ref. Gumprecht, loc. cit., No. 14.

† Op. cit., p. 158.

‡ 'Manchester Med. Chron.,' Jan., 1896.

Cholelithiasis is in all probability, then, the cause and not the result of primary cancer of the gall-bladder and bile-ducts.

**Arterial Sclerosis and Atheroma** are frequently associated with cholelithiasis, as is to be expected from the fact that all three are common affections of old age, and two or even all of them can easily occur coincidentally in the same subject. It is probable that there is some pathological condition of metabolism which is a common predisposing cause of all these three diseases.

Morgagni considered, from an experience of several cases, that gall-stones and urinary calculi were often caused by the same conditions, and some modern writers have occasionally met with cholelithiasis in association with nephrolithiasis. Such cases are, however, not at all common, and there is probably no general association between the diseases; but it is quite possible, judging from the frequent occurrence of lithates in the urine of gall-stone cases, that in the same patient, uric acid calculi may be formed in the urinary system as a result of the same cause which induces cholelithiasis.

A good instance of the association of the two diseases in one patient occurred in the Manchester Royal Infirmary, and was recorded by Wright.\*

The patient, a man aged 44, had complained for some time of symptoms of renal calculus, associated with pain about midway between the right kidney and the urinary bladder in front, and sometimes in the right loin. He had never had any symptoms of jaundice or any other liver affection.

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\* 'Lancet,' March 28th, 1885.

As the condition did not improve, the right kidney was explored through a lumbar incision, and was found not to be enlarged; but in it, near the pelvis, an abnormally hard spot could be felt. In the region of the groin, in which patient had felt much pain, a hard mass was discovered, which moved freely with respiration. It was with difficulty drawn up into the wound, when it was found to be the gall-bladder containing a calculus the size of a pigeon's egg. The concretion was removed, and the edges of the incision in the wall of the gall-bladder were stitched to the abdominal wound. As the situation in which the gall-bladder was found corresponded to the seat of the pain from which patient had suffered, it was thought unnecessary to examine the kidney any further. The patient died shortly after the operation, and a *post-mortem* examination was made. There were signs of recent acute general peritonitis. The liver was displaced and pulled downwards, so that its upper surface looked almost directly forwards. The gall-bladder was greatly increased in size, and the cystic duct was patent, but had probably been obstructed by the flexion to which it had been subjected by the abnormal position of the liver and gall-bladder. The liver and biliary passages were apparently healthy, and no other calculi were found. In the pelvis of the right kidney, corresponding to the hard mass felt during the operation, was a pyramidal calculus the size of a hazel-nut, composed of uric acid.

**Is Cholelithiasis a Constitutional Disease?**—Many writers, including some of the earliest and some of the latest authorities on the subject, consider that gall-stones frequently develop as the result of a constitutional peculiarity, which is present in certain people more than in others. They look upon the development of cholelithiasis as one form of the manifestation of a general diathesis, which may also be revealed by other affections somewhat allied in nature to cholelithiasis. Budd thought that a liability to gall-stones depended upon a peculiarity of constitution, which might be inherited or acquired, but of the nature of this diathesis he knew nothing beyond

the tendency which it manifested to cause fatty degeneration of the wall of the gall-bladder.

Bouchard and Chauffard\* consider the disease to be a constitutional condition allied in its nature to several other diseases which are more or less connected together to form one large group. The chief of these affections are acute articular rheumatism, diabetes, obesity, gout (hereditary or acquired), chronic rheumatic arthritis, asthma, migraine, neuralgia, and eczema.

Cholelithiasis occurs in one third of the cases of diabetes in women. Sénac met with hereditary or acquired gout 95 times, and with urinary gravel 98 times, in 166 cases of cholelithiasis (Chauffard\*). Bouchard† found chronic rheumatism 29 times, diabetes 16 times, gout 13 times, urinary gravel 18 times, marked obesity 15 times, and migraine 17 times, in 165 cases of cholelithiasis. In Bouchard's experience, obesity is present in 72 per cent. of the cases of the disease.

The parents of the subjects of gall-stones not uncommonly suffer from similar affections to the above. Thus in Bouchard's 165 cases there was a parental history of chronic rheumatism 19 times, diabetes 20 times, gout 25 times, cancer 10 times, and cholelithiasis itself 36 times.

Obesity, gout, diabetes, and to a certain extent chronic rheumatism frequently owe their origin to perversion of the nutritional processes of the body,

\* 'Traité de Médecine,' Charcot, Bouchard, and Brissaud, 1892, vol. iii, p. 720.

† Ref. Dufort, 'Rev. de Méd.,' vol. xiii, 1893, p. 286.

and it is quite possible that the form of cholelithiasis which arises without the presence of an acute infectious cholecystitis may be due in great part to the same cause.

The diathesis theory of cholelithiasis has very few, if any, advocates in Germany, and Naunyn does not believe in it. Charcot considers that the prevalence of cholelithiasis in old people is due chiefly to atony of the muscular fibres in the walls of the gall-bladder and large ducts which normally aid in the expulsion of the bile, causing a tendency to biliary stagnation. This muscular atrophy may also account for the freedom of old people affected with cholelithiasis from symptoms of the disease; for if there be not sufficient muscular force to expel the fluid bile, there can hardly be enough to move a calculus.

## CHAPTER IV.

Various Theories of the Mode of Origin and Development of Gall-stones: Coe, Budd, Frerichs, Thudichum—Naunyn's Views on the Subject—Biliary Stagnation—The Development of Cholesterin from the Desquamated Epithelium—Origin of Myelin Forms—First Appearance of Rudimentary Gall-stones; their Further Growth and Stratification—Crystals of Cholesterin embedded in the Wall of the Gall-bladder—Infection of Bile by Micro-organisms as an exciting cause of the Development of Gall-stones.

**Thomas Coe, M.D.**, made the first important attempt in England to deal with the subject of gall-stones, when in 1757 he published a book on 'Biliary Concretions.' A perusal of this work is most interesting, and some of the ideas and theories held by Dr. Coe have been but very little improved upon, even at the present day. I give a few extracts from his theories concerning the cause of the disease.

"When by any means the bile is retarded so as to stagnate, it is readily formed into biliary concretions. There are many causes which may contribute towards the inspissation and stagnation of the bile—declining age, sedentary or inactive life, a slower circulation of the blood, and the use of spirituous liquors. Gall-stones are oftener found in women than in men (five to one). Compressing the viscera is another cause. Angry passions and long-continued grief have a

wonderful effect upon the bile. But perhaps we should add to all these causes a peculiar disposition of the body, owing to circumstances which are not to be explained, for we do not see gall-stones bred in all who are old or inactive, and they are sometimes found in those who are not old nor want exercise."

In 1857 **Dr. Budd**, in the third edition of his work on 'Diseases of the Liver,' states his views as to the causes of the formation of biliary calculi. His conclusions are summed up in the following lines :

"Two circumstances seem then generally to concur in the formation of these cholesterin calculi. The first step is the formation of the nucleus which probably results from an unhealthy state of the bile, or from its decomposition or undue concentration in the gall-bladder, leading to precipitation of some of the essential principles of the bile or of some salts of lime in solid form. The second step is the formation of crystals of cholesterin. This may likewise result from an unnatural state of the bile, especially from a relative deficiency of taurocholate of soda, which seems to be the chief solvent of cholesterin in the bile, but it is frequently associated with and apparently dependent upon fatty degeneration of the coats of the gall-bladder."

"Gall-stones are frequently found in conjunction with cancer of the liver."

Budd describes one case in which the "cystic duct seemed to have been long blocked up by a stone, and the gall-bladder, whose coats had undergone the fatty degeneration, was filled with viscid mucus sparkling with scales of cholesterin." From this case he con-

cludes that an excess of cholesterin is not in itself sufficient for the formation of gall-stones.

A few other extracts from Dr. Budd's work will be of interest as showing the importance which he attaches to a pathological condition of the mucous membrane of the gall-bladder being the essential condition for an increased production of cholesterin.

"When the walls of the gall-bladder are much diseased, cholesterin is usually formed, or at least takes the solid form, in large quantity, and if there be a small mass of inspissated bile to serve as a nucleus, cholesterin collects around it and produces the more common kind of gall-stone. . . A particle of cholesterin may of itself serve as a nucleus of a solitary gall-stone.

"Gall-stones which are distinctly laminated have sometimes a crust of pure cholesterin which was formed after the entrance of bile into the bladder had been prevented by one of them becoming impacted in the cystic duct.

"When several gall-stones are found in the gall-bladder they all have the same characters, and were probably formed at the same time and not in succession."

Frerichs,\* in 1861, expressed his opinion that gall-stones arise from precipitation of their constituents from solution by decomposition of the bile. The chief cause of this decomposition is the acid condition which, he thinks, the bile assumes when a catarrhal exudation from the mucous membrane mixes with it. This acidity decomposes the bile salts into bile

\* 'Klinik der Leberkrankheiten,' 1861.

acids, which are insoluble in water. The cholesterin and other constituents of gall-stones which were held in solution by the bile salts, are then precipitated, and tend to form calculi. Frerichs believed that lime plays an important part in the formation of calculi, as he had on more than one occasion found evidence to suggest that it was secreted by the mucous membrane of the gall-bladder.

Frerichs does not mention any definite cause for the above inflammation of the biliary passages, otherwise his theory in great part is similar to the latest explanations of the inflammatory forms of gall-stone formation.

Thudichum,\* in 1863, attributed the formation of biliary calculi to a "decomposition of the bile akin to putrefaction, the compound amido- (bile) acids splitting up into their constituents under the influence of a cause which remains to be ascertained, but which is probably a putrid ferment absorbed from the intestinal canal. The cholesterin being dissolved by the taurocholate of soda is precipitated as soon as the bile salt is decomposed into the cholalic acid and glycin and taurin. The cholesterin once set free crystallises and deposits upon any particles that may happen to be within easy distance."

It is quite possible for such a sequence of events to take place in the bile, and the cholesterin would be deposited if the bile salts which dissolve it be decomposed into glycin and taurin and cholalic acid. Cholalic acid is almost insoluble in water, and there is no record of any experiments on its solvent capa-

\* Op. cit.

city for cholesterin. Being closely allied in properties to the biliary acids, it is probably like them not capable of dissolving cholesterin. On the other hand, if cholalate of soda be formed by the above decomposition, there need be no precipitation of cholesterin, as this salt is a good solvent (half the capacity of the bile salts—Minkowski\*) for cholesterin, and the fats and soaps present in the bile will further prevent precipitation.

Naunyn† has in recent years added to, and placed upon a firmer basis, our knowledge of the processes which lead to the formation of biliary calculi. He does not believe that a precipitation of cholesterin in the bile takes place during life as a result of the decomposition of the bile salts which hold it in solution, for one of the decomposition products—namely, the sodium salt of cholalic acid—is a good solvent for cholesterin. (This argument is not very sound, for cholalic acid is not a solvent of cholesterin, although its soda salt is, and the former is generally a result of the decomposition of a bile salt, and not the latter.)

Naunyn also thinks that the presence of a foreign body in the gall-bladder is not essential for the formation of a gall-stone, and that the presence of one does not of necessity cause a deposit of cholesterin. He arrives at these latter conclusions partly from the results of some observations carried out by Labes, who introduced various bodies, *e. g.* decomposing animal matter, acid and alkaline substances, and gall-stones, into the gall-bladders of dogs without finding

\* Ref. Gumprecht, loc. cit. † Op. cit., pp. 16—35.

that any deposit of biliary matter formed on them. The gall-stones even disappeared after a time. (Marcantonio\* found, however, that pieces of amber introduced into the gall-bladder of a dog became incrustated with a deposit of biliary matter.)

*Biliary Stagnation* is in Naunyn's opinion the first essential condition for the formation of gall-stones. This condition he thinks either has a directly injurious effect on the cells of the mucous membrane (bile contains a strong protoplasm poison), or the stagnated bile, becoming infected by micro-organisms, causes an inflammation of the mucous membrane lining the biliary passages, and thus indirectly leads to destruction of the epithelial cells. Whether affected directly or indirectly, the epithelial cells are shed into the bile, and there undergo further changes.

*The Development of Cholesterin from the Desquamated Biliary Epithelium.*—In young people these cast-off epithelial cells are pale, but in older people and those who have died of tuberculosis, acute febrile affections, or heart disease, and always where calculi already exist in the gall-bladder, the cells contain many fat globules and *myelin forms*. The latter have almost the same appearances as the bodies which I have described as forming when a solution of soap acts on cholesterin. These myelin forms exude or escape from the cells, and swim freely in the bile, either singly or in clusters. Naunyn describes the mass formed by a cluster of the myelin forms as being of a glassy, structureless nature, which in his opinion consists of cholesterin in a viscid form. From my

\* Ref. Gumprecht, 'Deutsch. med. Woch.,' 1895, No. 14.

own experience of these myelin forms, which I have observed very often in bile, and especially in that obtained from cases of mitral disease, I should say that they are of a very similar nature and composition to the myelin forms which I have previously described as resulting from the action of soap on cholesterin. Naunyn considers that the above-mentioned soft, amorphous, cholesterin masses are one form of *rudimentary gall-stones*, and he also describes another form of rudimentary stone, which consists of cholesterin in a hard, vitreous, amorphous condition, but which sooner or later shows evidence of crystallisation. This latter hard variety is also, he thinks, derived from the myelin forms ; and not uncommonly such a small hard rudimentary gall-stone contains a centre of a brownish pulpy mass, consisting probably of bilirubin-calcium and biliary detritus, in which again may be found a hollow space. The process which results in the formation and precipitation of bilirubin-calcium in the bile is uncertain, but Naunyn considers that it is possibly one of an inflammatory nature, in which an exudation takes place of an albuminous secretion from the inflamed mucous membrane, containing perhaps some lime salts, which causes the formation of the insoluble pigment compound, for bilirubin unites with calcium somewhat readily in the presence of albumen. I have myself frequently seen both the soft and hard forms of amorphous cholesterin occurring with the clusters of myelin forms, but I think that rudimentary calculi can arise in yet another way. I have explained previously how the soap-cholesterin bodies under the

action of water lose their compound nature, and are broken up, the cholesterin being deposited in the crystalline form. I have very frequently watched the myelin forms in bile from day to day, and have seen how they gradually disappear, and how crystals of cholesterin develop with great rapidity and in great profusion, and the question occurred to my mind as to whether the crystals which form in bile might not be deposited from the myelin forms by a process analogous to that which leads to their formation from the soap-cholesterin bodies. This process may of course take place, whilst that described by Naunyn is going on.

When many crystals of cholesterin are present in the bile, they lie together in clusters in which the individual crystals are cemented together by a brown pasty material. Such a conglomeration forms the basis from which a large calculus may grow by the deposition on it of cholesterin in the crystalline form, and of biliary pigment derivatives. Any number of these elementary conglomerations may form at the same time in the gall-bladder, and each one be the nucleus of a gall-stone.

Chemical analysis of the above concretions shows the presence in them of cholesterin, fat, bilirubin-calcium, bile salts and albuminous substances in varying proportions. Free bilirubin is only found in traces in them (Naunyn).

*Further Growth of all the forms of Rudimentary Gall-stones* takes place by the addition, in layers, of material similar to that of which they already consist—generally bilirubin-calcium and cholesterin.

Cholesterin also frequently enters, whilst it is in a viscid or fluid condition, into the body of a concretion by a process of infiltration through small pores or canals, and assumes a crystalline condition afterwards. Such an infiltration-process most frequently takes place in amorphous, pasty conglomerations, chiefly composed of bilirubin-calcium, which, in consequence, become of a more firm, crystalline structure. Soft concretions are squeezed into more compact masses by contraction of the gall-bladder, which, whilst it expels the fluid bile, is unable to dislodge the solid body. In the same way several concretions may be welded together to form a mulberry-shaped mass. Concretions which are found in the intra-hepatic ducts frequently have the appearance of being composed simply of inspissated bile, but Naunyn thinks that they cannot be formed in this way as they consist largely of bilirubin-calcium, and this compound is not produced by simple inspissation of the bile. They also often contain products of the higher oxidation of bilirubin. The cause of the formation of these intra-hepatic calculi is uncertain, but it may be due to an inflammation allied in character to that which takes place in the gall-bladder and larger ducts, and results in the development of gall-stones.

*The Stratification of Calculi* is an interesting process. The layers may consist of pure white cholesterin, or of a mixture of cholesterin and bilirubin-calcium. They are of different thicknesses, varying from less than a millimetre to more than five millimetres. Bilirubin-calcium layers can only be added to a concretion in the gall-bladder so long as bile is able to enter

through the cystic duct. Cholesterin layers can, on the other hand, be added if the cystic duct be closed, or if the concretion lie in a recess in the wall of the gall-bladder or large bile-duct. Alternating layers of pure cholesterin and bilirubin-calcium are deposited when the bile enters the gall-bladder and remains there for a time, is then expelled, and cannot make its way in again for a lengthened period, owing to some obstruction of the cystic duct of an intermittent nature.

### **Crystals of Cholesterin in the Wall of the Gall-bladder.**

I have previously mentioned two cases which I met with myself, and also one recorded by Bristowe (see p. 22), in which crystals of cholesterin were found embedded in the wall of the gall-bladder. The appearance of these rudimentary gall-stones, lying in what seemed to be retention-crypts of the mucous membrane, suggested to my mind the possibility that some of the glands in the wall of the gall-bladder might, under certain conditions, secrete cholesterin in a fluid or viscous form, and pour it out into the cavity of the organ. If there be an insufficient quantity of solvent media in the bile to take up the cholesterin thus formed it will undergo crystallisation, and form the basis of a gall-stone like that which results from the changes in the myelin forms. It is also possible that the crystalline masses of cholesterin, which form in the mucous crypts, escape from the spaces in which they lie into the cavity of the gall-bladder, and appear in the bile as fully-developed rudimentary gall-stones.

My observations on the development of crystals of cholesterin in human bile, obtained after death, are not incompatible with the above suggestion; for although I have followed the various steps in the changes from epithelial cells to cholesterin crystals described by Naunyn, and referred to on a previous page, I never was able to satisfy myself that the myelin forms were present in large enough quantities to account for the innumerable crystals of cholesterin which eventually developed.

Thinking it possible that cholesterin might be already present in a viscid form or in solution in the bile when the epithelial cells abounded and no crystals could be seen, I endeavoured to separate the cells from the fluid portion of the bile in a centrifugal apparatus, but was unable to do so owing to the thick, viscous nature of the bile. My suggestion that some of the glands of protective mucous membranes may excrete cholesterin in a viscid form, or some body closely allied to, and which is converted into the latter substance under certain conditions, is also supported by the fact that I have never seen any of the myelin forms in bronchial mucus in which crystals of cholesterin appear after inspissation of the mucus has taken place.

### **Infection of Bile by Micro-organisms as an Exciting Cause of the Development of Gall-stones.**

At the commencement of the account which I have given of Naunyn's views on the formation of gall-stones, it was mentioned that he considered the presence of biliary stagnation essential for the produc-

tion of the material necessary for the development of the calculi. He states that bile contains some body which acts injuriously on living protoplasm, and which causes the death of the cells of the biliary mucous membrane if it remains in contact with them for an abnormally long time. The cells thus injured are cast off into the bile, where they undergo further changes, resulting in the formation of cholesterin, and probably also of bilirubin-calcium. In addition to this somewhat passive process of cell-destruction, it is very probable that a more active inflammatory condition of the mucous membrane, resulting also in the profuse destruction and desquamation of its cells, is set up at times by the entrance of infectious micro-organisms into the bile whilst it is in a state of stagnation in the biliary passages. The inflammation of the mucous membrane thus set up, which results in the formation of those materials necessary for the development of gall-stones, may be spoken of as a "stone-forming catarrh." This question of the infection of bile by micro-organisms is an interesting and important one, and will require to be considered rather fully. Normal bile contained in the biliary passages of healthy men and animals which empty periodically is sterile (Gilbert and Girode,\* &c.). Frequent inoculation experiments on animals have proved this, and the not uncommon event of healthy bile escaping into the human peritoneal cavity without doing any injury to the peritoneum, points to the same conclusion.

\* 'Comptes rend. de la Soc. de Biol.,' 1890, No. 39; and 1891, No. 11.

When, however, the biliary passages are in a pathological condition, micro-organisms readily enter and infect the bile either from the blood or from the duodenum. Sherrington\* thinks that though the blood be teeming with micro-organisms none can escape through the normal living hepatic tissues, and it is only when the latter have been damaged by toxins in the blood, formed by the life of the bacteria, that the tissues allow the germs to pass through them. Nor can the germs enter the common bile-duct from the duodenum, where they abound, so long as the subject remains healthy and the bile be normal in constitution and expelled regularly. When, however, the flow of bile from any cause becomes obstructed, and the bile stagnates, then the micro-organisms invade it at once from the intestine.

Normal bile, though aseptic, is by no means antiseptic, and will not prevent the growth of micro-organisms which enter it. On the other hand, a strong solution of the bile salts is undoubtedly antiseptic.

The appearance of micro-organisms in stagnant bile has been verified experimentally in animals by several observers.† Charcot and Gombault found that after ligature of the common bile-duct in dogs, the bile in the ducts above the ligature became infected, and Netter was always able to cultivate bacteria from the bile of dogs obtained from the passages above a similarly placed ligature, and about

\* "Experiments on the Escape of Bacteria with the Secretions," reprint, 'Journ. Path. and Bact.,' 1893.

† Ref. Naunyn, op. cit., pp. 43, 44.

twenty-four hours after the operation. In such cases he found staphylococci and bacilli. The bacillus most commonly met with in infected bile is the *Bacterium coli commune*. Gilbert and Girode cultivated the latter organism from bile taken from the bile-ducts of a man twenty-four hours after death, and many other observers have obtained similar results.

Naunyn\* injected the *Bacterium coli commune* into the gall-bladders of healthy dogs after he had previously caused biliary stagnation by ligaturing the common bile-ducts low down, and found that the animals soon died with symptoms of general septic infection and local evidence of an acute cholangitis.

Netter† and other observers found staphylococci and streptococci present in pathological human bile. Martha,† Gilbert and Girode,‡ Bouchard,§ and others have also studied this subject closely, and have found the *Bacterium coli commune* in the bile of cases of inflammation of the biliary passages (cholangitis).

Naunyn also obtained the same bacillus by puncture of the gall-bladder during life in five cases of cholecystitis, which he thinks were of recent occurrence, and which were ushered in by undoubted attacks of biliary colic.

Chiari|| found the typhoid bacillus in the gall-bladder in 19 out of 22 cases of enteric fever, and Dufort,¶ Bernheim, and Hagenmuller are of the

\* Op. cit., p. 46.

† 'Arch. de Phys. norm. et Path.,' 1886, p. 7.

‡ 'Comptes rendus Société Biol.,' 1890, 1891.

§ Ibid., 1890.

|| 'Prag. med. Woch.,' 1893.

¶ 'Rev. de Méd.,' 1893, p. 281.

opinion that cholelithiasis is not an infrequent sequela of enteric fever.

In the face of the above evidence there can be little room for doubt that micro-organisms readily invade the bile in the biliary passages when it is in a state of stagnation, and excite an inflammation of the lining membrane of the ducts (cholangitis) and of the gall-bladder (cholecystitis). As biliary stagnation frequently results from the obstruction to the outflow of bile caused by a calculus in the common bile-duct, it is almost certain that infection of the bile may also follow frequently on biliary obstruction from the same cause, but whether the invasion by micro-organisms of bile which has become stagnant from other causes than an obstructing gall-stone, can result in the formation of biliary calculi is quite another matter. In Naunyn's opinion there are two points which seem to favour the view that the latter event is possible. In the first place, putrefactive bacilli can cause a precipitation of bilirubin-calcium, and it is possible that other forms of bacilli may do so as well. In the second place, he has found micro-organisms in the centre of a few bilirubin-calcium calculi. The latter occurrence is, however, rare, and, as a rule, bacilli have not been found even in young concretions, nor in those consisting of pure cholesterol.

If the presence of micro-organisms is an exciting cause of the formation of biliary calculi, it probably acts by the bacilli setting up a stone-forming catarrh of the mucous membrane of the biliary passages.

It is very probable that the bile is at times infected

by micro-organisms without there being any local or general symptoms to indicate an abnormal condition of affairs. Thus Naunyn withdrew some of the contents of a dilated gall-bladder of three months' standing, and cultivated from the fluid the *Bacterium coli commune*. Dupré\* recorded a case in which febrile cholelithiasis developed four months after recovery from a severe form of typhoid fever. A pure cultivation of the typhoid bacillus was obtained from the contents of the inflamed gall-bladder.

Létienne† inoculated tubes with bile obtained immediately after death from forty-two patients, and found it infected in twenty-four instances by micro-organisms, including the *Bacterium coli commune* and streptococci. There had been no indication of biliary infection in any of the forty-two cases during life. Létienne's results are very unsatisfactory, however, as the bile could easily become stagnant whilst a patient was moribund, and allow the entrance of micro-organisms, which are notorious for their powers of travelling rapidly.

Although micro-organisms may at times play an important part in exciting the formation of gall-stones, their presence in bile is in all probability not essential for the development of the disease. A point which supports this latter conclusion is, that gall-stones occur so very frequently in old people without exciting any symptoms either of hepatic or of other ailments. One can hardly imagine how such could be the case

\* Ref. Gumprecht, 'Deut. med. Woch.,' 1895, No. 14.

† 'Arch. de Méd. Experim.,' 1891.

were the disease always excited by the development of an infectious condition of the bile or of a cholecystitis.

Like many other points in connection with cholelithiasis, the exact part which is played by micro-organisms in the causation of the disease is very uncertain, and until more knowledge is obtained, the question as to whether the infection of stagnant bile by micro-organisms is the cause or the result of the formation of gall-stones must be considered as one which is still *sub judice*.

Whatever the pathological cause of the stone-forming affection of the biliary mucous membrane may be, the process which leads to the formation of gall-stones is often, very probably, of a temporary or acute nature, and excites the rapid and synchronous development of many calculi. Budd was of this opinion, which he formed, in great part, from the fact that multiple calculi have almost always the same physical appearance and chemical characteristics, and look as if they were all formed by the same process and at the same time.

In other cases, especially in old people, the process is probably of a much more gradual and chronic nature, the gall-stones increasing in size slowly as long as the patient lives.

## CHAPTER V.

Concluding Remarks on the Causes leading to the Development of Gall-stones—Cholesterin in Cholelithiasis is Derived from the Mucous Membrane of the Biliary Passages—An Increased Quantity of Cholesterin is formed in Old Age—Catarrhal Conditions of the Biliary Mucous Membrane—The Formation of an Abnormally Small Quantity of Bile Salts may result in the Development of Crystals of Cholesterin—Causes leading to a Deficient Formation of Bile Salts — Gall-stones, Gout, and Lithiasis—Summary.

**Concluding Remarks on the Development of Gall-stones.**

There are some points which appear to me to be worthy of attention when considering the causes leading to the development of that form of cholelithiasis in which more cholesterin is formed than can be held in solution in the bile.

I have brought forward evidence in previous pages which to my own mind proves, almost conclusively, that *cholesterin is derived from the mucous membrane* lining the biliary system, in normal, but more especially in abnormal states of the body. In the ordinary course of events the bile contains sufficient material to dissolve the cholesterin and hold it in solution, but it may happen either, that more cholesterin is formed than the normally constituted bile can dissolve, or that with a normal amount of cholesterin the bile contains an insufficient quantity of solvent

media to hold it in solution. In either case the excess of cholesterin will tend to crystallise out and form a solid deposit in the bile. There are certain points in connection with both the above causes of the precipitation of cholesterin in the bile which seem to me to be of importance.

*An increased quantity of cholesterin* is formed normally, so to speak, in old age, and abnormally in some constitutional conditions, and as a result of certain catarrhal inflammations of the biliary mucous membrane, probably excited by the entrance of micro-organisms into bile which is in a state of stagnation. Biliary stagnation is not essential for the formation of calculi in old people, although it is probably present to a certain extent in many of this class of subjects, but the crystals in which the excess of cholesterin appears, may remain behind in the dependent fundus of a gall-bladder which is able to contract well enough to expel most of its fluid contents. Such a collection of crystals, bound together by a pasty mass of biliary detritus, forms the starting-point of a gall-stone. The nucleus of a concretion may also be provided by the escape of one of the crystalline cholesterin masses, which I have described as forming in the wall of the gall-bladder, from its birthplace into the cavity of the organ, where it will increase in size by the deposition on it of the cholesterin which is present in excess in the bile. The purer forms of cholesterin calculi probably originate and grow in either or both of the above ways, which are of a chronic nature as compared with that connected with inflammatory processes.

The catarrhal condition of the biliary mucous membrane excites an acute formation of an excess of cholesterin, and by the inflammatory exudation which is secreted at the same time, the formation and precipitation of bilirubin-calcium is induced, which unites with the cholesterin to form the mixed types of calculi.

Those calculi which consist of pure bilirubin-calcium are probably formed as the result of an inflammation of the biliary mucous membrane, which leads to the secretion of an inflammatory fluid without the formation of an excess of cholesterin. The inflammatory fluid excites the formation of the bilirubin-calcium compound.

In both the normal and abnormal production of an increased quantity of cholesterin, the bile may contain an amount of substances—fats, soaps, but especially bile salts—which is capable of dissolving a normal quantity of cholesterin, but which cannot prevent the crystallisation of an excess of the latter substance.

*The Formation of an abnormally small Quantity of Bile Salts*, irrespective of the fats and soaps in the bile, may, in my opinion, have some influence on the crystallisation of cholesterin. If an increased amount of this latter substance be formed, it stands to reason that a supply of bile salts sufficient to dissolve it would tend to prevent its crystallisation. And in the same way, with a normal amount of cholesterin present, there would be a tendency for crystals to form, if the bile salts were present in abnormally small quantity. A deficient supply of bile salts might arise in two ways.

*Causes leading to a Deficient Formation of Bile Salts.*

—(1.) I have shown from the researches of different authorities (especially Spiro and Noël Paton) that more bile salts are formed when an animal is fed on a nitrogenous diet than when fed on non-nitrogenous food. A similar relation between the diet and the formation of bile salts probably exists in man, and I think that there are some points connected with the prevalence of gall-stones in certain classes of people which not unreasonably suggest that diet may have more to do with the development of the disease than is generally believed to be the case.

Gall-stones occur much more frequently in old people and females than in young people and males. The diet of the former classes is more non-nitrogenous in nature (carbohydrates, fats, and sugars) than that of the latter, for men and young people require much solid nitrogenous food to enable them to live their more arduous and active lives.

The disease is more prevalent in Germany than in England. The English are greater meat-eaters than the Germans are, the relative amount of nitrogenous foods in the typical diets of the two nations being expressed in a way in that allowed to the soldier—the German receiving 6 ounces of meat, whilst the Englishman receives 12.

Gall-stones are very rare, according to Hirsch, in Eastern nations, only one or two cases of calculi occurring in natives of India having been recorded. There the staple food is rice, with 7·4 per cent. of nitrogenous constituents, or millet, with 11·3 per cent. Both these amounts are much lower than that

contained in meat, but a regular and large quantity of the food is consumed.

The above facts favour the view that gall-stones tend to occur more readily in people who eat less of nitrogenous foods than in those who live on a highly nitrogenous diet. More bile salts are formed from the latter dietary than from the former, and so a person living on a nitrogenous diet would have more bile salts present in his bile to dissolve the cholesterolin than would one living on a non-nitrogenous diet.

(2.) A deficiency of bile salts in the bile may also arise from a pathological condition of the liver preventing their formation by the hepatic cells, although the materials necessary for their formation are present in quantity in the blood.

Physiologists think that the bile salts are normally formed in the liver cells by the union of glycine and taurine with cholalic acid, bodies which are already present in the blood when it reaches the liver. They also believe that the liver excretes from the blood of the portal vein a certain amount of the fully-formed bile salts which have passed into the portal system from the intestine.

A derangement of the liver, the exact nature of which I cannot say, might easily interfere with this normal process of secretion and excretion of bile salts, in the same way that certain hepatic disorders interfere with the formation of urea in cases of gout or urinary lithiasis. It is also probable that the same derangement of the liver may result in the synchronous development of gout or lithiasis and cholelithiasis.

At any rate, it is very common to find lithates present in quantity in the urine in cases of gall-stones, and in certain forms of chronic heart disease in which the urine contains copious deposits of urates, gall-stones are very often met with. The latter of these two conditions is common in patients below thirty, a period of life in which the appearance of cholelithiasis unassociated with other diseases is very rare.

*Gall-stones and Gout and Lithiasis.*—Many observers consider that there is a connection between cholelithiasis and gout or urinary lithiasis, and that these affections may be excited by the same cause. The connection between gout and lithiasis and gall-stones may be explained theoretically in three ways: (a.) In the formation of uric acid in the liver some of the glycine which ought to go towards forming glycocholate of soda combines with two molecules of urea and forms a forerunner of uric acid (Latham's\* theory), thus diminishing the amount of the bile salt formed. This reaction does take place in a test-tube. (b.) The pathological state of the liver which leads to the imperfect formation of urea may also prevent the formation of the bile salts. (c.) The treatment of gout in reducing the nitrogenous diet diminishes the foods from which bile salts are derived.

In England it is thought by many that gall-stones occur more commonly in the wealthy than in the labouring classes, but statistics concerning the frequency of the disease in the former class are impossible to obtain. The men of both classes live on a diet containing much nitrogen, but the wealthy feed

\* 'Lancet,' 1884, vol. i, p. 485; 1885, vol. i, p. 1120.

their palate rather than their muscles, and the "rich" methods of preparing their food, together with the amount of alcohol taken with it, induce the morbid hepatic state which results in the formation of uric acid, and inability on the part of the cells to unite the glycine and taurine with the cholalic acid to form the bile salts, or to excrete from the blood of the portal vein the already-formed bile salts which have been reabsorbed from the intestinal contents.

Should the morbid liver cells form the bile acids instead of their sodium salts, the mischief is done, for the latter are the solvents of cholesterin in the bile, and the acids, being themselves scarcely soluble in water, do not dissolve it at all.

*Summary.*—I believe, then, that in certain conditions of the body there is an increase in the amount of cholesterin produced by the mucous membrane of the biliary passages, and that in others there is a diminished amount of bile salts formed by the liver.

When the first of the above conditions is present, the bile salts may be formed in normal quantity and yet be unable, even with the help of the fats, soaps, and fatty acids which are also contained in the bile, to hold the extra cholesterin in solution, so that some of the latter is deposited in a crystalline form, and a nucleus for the formation of a gall-stone is provided. By this sequence of events the origin of chronic latent cholelithiasis of old age is induced. I am strongly of the opinion that there is naturally an increased tendency to the formation of cholesterin in old age, which is much more marked in some people than in others. It is probably due to degene-

rative changes, the exact nature of which is, however, hard to explain. When the bile salts are formed in diminished quantity owing to an insufficient consumption of nitrogenous food the disease will also, probably, run a chronic course, but if derangements of the liver be the cause of their inadequate or incomplete formation, the symptoms of cholelithiasis are of a more acute nature, for the same pathological condition of the body which leads to the hepatic derangements will also probably induce a morbid condition of the mucous membrane of the gall-bladder which results in an increased production of cholesterin. With an increased formation of cholesterin taking place at the same time that a diminished quantity of bile salts is being produced, abundant material is provided for the rapid growth of gall-stones.

Biliary stagnation, with the consequent infection of the bile, probably, at times, plays an important part in the formation of gall-stones. The mode of action of this process is not definitely known, but it is probable that the infection of the bile sets up a stone-forming catarrh of the mucous membrane of the gall-bladder, which results in an increased production of cholesterin. The micro-organisms may also cause decomposition of the biliary salts and render the bile incapable of dissolving its normal amount of cholesterin. The advocates of this theory also look upon the bile salts, as I have done, as the all-important constituents of the bile for the solution of cholesterin, and do not take the fats, soaps, and fatty acids into consideration.

The presence of bile salts also prevents the combi-

nation of bilirubin with calcium, the product of which is frequently the starting point for the growth of calculi.

I am fully aware that my views on the determining causes of the formation of gall-stones are eminently theoretical, and have but a slender basis of facts, but the advocates of other ideas are no better off in this respect.

The actual knowledge of the pathological processes which result in the development of cholelithiasis is still very rudimentary, and there is room for much more clinical and pathological investigation in man on the subject.

## CHAPTER VI.

Varieties of Cholelithiasis—Transitory and Chronic, Regular or Uncomplicated, and Irregular or Complicated Cholelithiasis—Regular or Uncomplicated Cholelithiasis—The Exciting Cause of its Symptoms—Life-history of Biliary Concretions—Latent Calculi in the Gall-bladder—The Migration of Concretions; their Escape from the Biliary Passages *per vias naturales*—The Size of Calculi which can Escape from the Bile-ducts *per vias naturales*—The Forces concerned in the Expulsion of a Stone from the Biliary Passages.

CHOLELITHIASIS may appear as a temporary or transient, and as a chronic disease. *Temporary cholelithiasis* is the more common of the two types of the disease, and is manifested clinically by what are called “attacks” of cholelithiasis, or more popularly, of gall-stones, which are set up, as will be explained later on, by the attempts made by a gall-stone to escape from the biliary passages into the intestinal tract. This escape of a calculus is very often effected after a period of time which varies from an hour or less, up to a day or two, and then the attack is over, and the patient may be quite free from the disease in the future, or, as frequently happens, may be subject to a recurrence of the attacks. The relapses take place after a more or less prolonged interval of good health.

In the *chronic form* of the disease the gall-stone is unable to effect its escape for a much longer time, or else no sooner has one calculus passed out of the biliary passages than another begins its journey through them, with the result that the patient is troubled with symptoms of the disease for months or even years.

The nature and severity of the attacks of gall-stones vary very much. Roughly speaking, there are two main classes into which all the attacks can be divided. They are termed regular or uncomplicated cholelithiasis, and irregular or complicated cholelithiasis.

*Regular or Uncomplicated Cholelithiasis.*—In the first of these groups are placed all those cases in which, after varying lengths of time, the disease tends towards temporary or permanent recovery without the onset of any serious complication, or without leaving behind any injury to the biliary system or to the body generally. In nearly all these cases recovery may be brought about by nature's unaided efforts, the disturbing elements passing out of the body *per vias naturales*. Recovery, as a rule, takes place in all these regular cases, but the attacks frequently recur.

*Irregular or Complicated Cholelithiasis* is a much more serious condition, for in it the original disease causes temporary or permanent injury to the body, or sets up some severe complication which frequently results in the death of the patient.

### Regular or Uncomplicated Cholelithiasis.

It will be advisable in the first place to consider the regular and uncomplicated affection. The latter adjective is a more accurate description of this simpler form of cholelithiasis, for although no complications supervene, and the course of the disease follows along the same broad lines, the symptoms which it causes are by no means regular in their appearance, but often vary very much in different cases, and even in different attacks in the same patient.

The *exciting cause of the symptoms* which are recognised as indicating an attack of cholelithiasis or of gall-stones is the attempt, on the part of a concretion which has been formed somewhere in the biliary system, to pass along the larger ducts and escape into the duodenum. When a gall-stone leaves the biliary system in this manner without causing any injury, it is said to pass out *per vias naturales*.

### The Life-history of a Gall-stone.

A short account of the life-history of biliary concretions will be of interest here, and will make future references to the various phases of the disease clearer. The life-history of a gall-stone may be divided into four stages. These are—

- (1.) The period of its origin and development.
- (2.) A longer or shorter period during which the stone lies quietly, or is latent, in the seat of its development.

(3.) The active period, during which the stone attempts to pass out of the biliary system and, as a rule, into the bowel.

(4.) The period of its existence outside the biliary system, and of its final expulsion from the body.

It is in the third stage of its life that a gall-stone excites those symptoms which indicate that the patient is undergoing an attack of cholelithiasis, and it is generally only during the last two periods that any symptoms at all indicative of the disease develop.

Some writers have described symptoms which in their opinion occur during, and are due to, the act of formation of gall-stones. The symptoms so described are, however, typical of chronic gastritis, and probably are excited by this affection, which certainly at times does accompany the development of gall-stones.

If patients have suffered from previous attacks of biliary colic, it is quite possible for them to recognise premonitory signs of another attack coming on, and symptoms of a cholecystitis which may result in the formation of biliary calculi, are met with at times, but in the majority of cases the origin and development of gall-stones takes place without exciting any recognisable symptoms. Developing biliary calculi are then almost invariably, so far as is known at present, of no clinical importance.

*Latent Calculi in the Gall-bladder.*—When a concretion has grown to a certain size its presence in the gall-bladder, whilst it still remains in a latent condition, may be revealed in one or two ways. If the calculus be very large, a distinct, hard tumour in the

region of the gall-bladder may be palpated during life, or it may excite sensations of uneasiness which cause a good deal of distress to the patients.

Coe\* relates one or two interesting cases of this nature. In one which occurred in the experience of Lentilius a tumour was felt in the right hypochondrium. Many things had been tried as cures, but to no purpose. At length a hepatic purging infusion was given, after which three hundred concretions were voided, the tumour subsided, and the patient got well. Cases have been recorded in which in thin patients the stones were felt like nuts in a bag, and sounds caused by the movements of the stones against each other can be heard at times with a stethoscope placed over the gall-bladder. One old physician, Fabricius Hildanus, tells of a case in which a man had for many years noticed a great weight falling from side to side under the liver as he turned himself in bed. In his gall-bladder were found *post-mortem* two large stones, one of them being one and a half inches in diameter and three inches in length.

Large calculi in the gall-bladder have also, now and then, been found *post-mortem* in cases in which during life the patients had complained of vague, severe pains which they could not definitely localise, and for which no cause could be determined.

*The Migration of Concretions.*—The migratory stage of a gall-stone's life-history is most important. The natural tendency of a concretion lying in the biliary passages is, up to a certain stage of its growth, to move on towards the outlet for the bile into the

\* Op. cit.

duodenum, provided of course that the bile itself be moving in its normal direction. Any concretion which has a smaller diameter than that of the orifice of the ostium duodenale of the common duct will pass out readily in this way, or, as it is called, *per vias naturales*. The escape of such a small concretion may cause no symptoms at all, or it may set up a reflex spasm of the muscular fibres in the ostium duodenale, and cause pain. There must, however, be a limit to the size of the calculus which can pass in the above manner through the narrow outlet of the common bile-duct, and any stone which requires force greater than that concerned in the normal expulsion of bile to enable it to pass into the duodenum will set up an abnormal condition of affairs, and excite the appearance of definite symptoms. The normal diameter of the ostium duodenale of the common bile-duct is less than one sixth of an inch, but the muscular sphincter which surrounds the orifice is capable of a certain amount of dilation.

*The Size of Biliary Concretions which can escape from the Bile-ducts "per vias naturales"* is variously stated by different observers. It is evident that only the very smallest hard calculi can escape through such a narrow outlet from the common bile-duct without causing symptoms, probably none larger than a very small pea; but it is possible for larger soft concretions, which can be moulded into a mass of small diameter, to pass out unsuspected. Firm calculi of larger size can in time be forced through the ostium duodenale without injuring it, but much pain is generally excited during the process.

The smallest concretions, known as biliary sand, may cause a good deal of pain during their escape into the duodenum, by irritating the mucous membrane and setting up a reflex spasm of the biliary muscle.

The size of the larger calculi which may be forced through the ostium duodenale of the common bile-duct by the passive stretching of the tissues surrounding it, is very difficult to determine. Some observers state that calculi the size of a hazel-nut can escape in this way, whilst others do not believe that any larger than peas can do so. There is an important source of error to be avoided in estimating the width of the ostium duodenale when examined *post-mortem* in man, for it has been shown by Roth\* that calculi very frequently cause erosion of the tissues surrounding this orifice, and give it the appearance of having been simply dilated, instead of having been enlarged by destruction of tissue. This will be referred to again later on. Altogether, judging from the narrowness of the normal bile-ducts and of the ostium duodenale in man, it is very improbable that calculi larger than peas can escape without injuring or eroding the latter, at any rate in the first attack of colic. In subjects who have suffered from several attacks of gall-stones, it is quite probable that the biliary passages will become dilated and allow of the escape of larger stones than could pass in a first attack. The ducts themselves are more dilatable than the ostium duodenale, and calculi up to the size of hazel-nuts are able to pass along with some trouble

\* Ref. Naunyn, op. cit., p. 79.

even during first attacks. The recurrence of the passage of large calculi through the ducts will cause their permanent dilation. The ostium duodenale is the narrowest portion of the extra-hepatic biliary system, and then follows the cystic duct; the hepatic and common ducts are of about the same diameter as each other.

### **The Forces Concerned in the Expulsion of a Stone from the Bile-ducts.**

A concretion which is endeavouring to escape from the biliary passages excites the development of two conflicting forces, one helping and the other hindering its expulsion. The force opposing the escape of the stone depends upon the size, shape, and consistency of the concretion, upon the width and capacity for dilation of the passages along which it moves, and also upon the strength of the forces which endeavour to promote the escape of the stone. A smaller amount of expulsive force is necessary to enable a soft, easily moulded concretion to pass out from the biliary passages, compared with that required for the escape of larger, hard calculi. The forces which tend to push on a gall-stone are those concerned in the normal expulsion of bile. They are—

(1.) *The Pressure under which Bile is Secreted.*—This force is but slight, being on an average not more than equal to that exerted by a column of mercury 24 mm. high.

(2.) *The Contraction of the Muscle Fibres in the Walls of the Gall-bladder and Bile-ducts* plays an important part in the onward movement of a gall-

stone. By this means the pressure of the bile in the ducts is temporarily raised, and remains high as long as the contraction persists. The presence of a stone irritating the mucous membrane sets up these contractions at the point of irritation, and probably also very markedly on the liver side of the impacted stone. At any rate, Naunyn\* found that when he stimulated electrically the mucous membrane of the common duct in live animals the muscle fibres in the wall contracted most vigorously one centimetre above, *i. e.* on the liver side of the irritation. Laborde† found when he introduced a foreign body into the common bile-duct of a dog that it was seized and held fast by the duct wall.

In old people the muscle fibres in the wall of the biliary passages atrophy and greatly diminish the expulsive power of the biliary system.

(3.) *The Movements of the Diaphragm and of the Abdominal Muscles* by exerting pressure on the liver, also raise temporarily the pressure in the ducts. Severe and sudden movements of the muscles of the anterior abdominal wall have, at times, been known to cause rupture of the wall of a duct or of a gall-bladder which has become distended behind an impacted stone.

The above expulsive forces, besides tending to move a gall-stone on through the bile-ducts, frequently cause a pathological dilation of the ducts behind the obstruction, even up to the intra-hepatic branches. Such dilation may eventually involve the duct immediately at the seat of impaction, and

\* Op. cit., p. 60.

† Ibid., p. 57.

thus allow of the escape of some bile alongside the stone, and so cause temporary relief of the symptoms of obstruction.

A return of the original symptoms will, however, take place when the obstructing stone is moved through the newly-dilated portion of the duct and engages in the narrower passage beyond. The ducts on the duodenal side of a completely impacted stone frequently contract greatly, and in cases of long duration their lumen becomes almost obliterated, a condition which adds greatly, of course, to the difficulty of further movement of the obstructing stone.

*The Forces which Oppose the Escape of a Gall-stone* through the bile-ducts are due to the resistance which the wall of the duct offers to being stretched beyond its normal capacity, and to the reflex spasm of the muscle fibres in the wall of the duct excited by the irritation of the mucous membrane by the calculus. The reflex spasm narrows the lumen of the duct around the calculus, and the wall of the duct grips and holds the irritating body tightly. This form of resistance to the passage of a biliary calculus through a duct is more of an active nature than that afforded by the stretching and dilation of the duct wall which result from a stone of larger diameter than the lumen of the duct being forced along it under pressure.

It is difficult to say whether the smoothness or the irregularity of the surface of biliary calculi diminishes, or adds to, the difficulties of their passage. Rough concretions are frequently passed without any difficulty, and smooth stones often cause much trouble ; or the reverse of this may happen. It is impossible to

make definite statements concerning the capacity for dilation of the normal biliary passages from *post-mortem* observation, for the condition of the tissues is then not comparable with that during life. The conflict between the forces which aid in, or resist the passage of, a gall-stone along the biliary passages, results in the development of several symptoms and physical signs which will be referred to in the next chapter.

## CHAPTER VII.

The Symptoms of Regular or Uncomplicated Cholelithiasis—Pain or Biliary Colic: its Character, Situation, Duration, and Causes—The Severity of the Pain is no Indication of the Severity of the Case—The Causes which Excite an Attack of Biliary Colic—The Impaction of Gall-stones in the Biliary Passages—The Escape of Gall-stones into the Intestines—Gall-stones Found in the Fæces—Jaundice: its Causes and Duration—Absence of Bile from the Stools, and its Effect on the Action of the Bowels—Bile Pigments in the Urine—Itching—Gastric Symptoms: Vomiting, Hæmatemesis, Derangements of Digestion—Enlargement of the Liver: its Physical Signs and Pathology—Enlargement, by Distension, of the Gall-bladder: its Causes, Physical Signs, the Nature of its Contents, and Diagnosis—The Temperature in Regular Cholelithiasis—The Cardio-vascular, Pulmonary, and Nervous Symptoms in Cholelithiasis—The Urine in Cholelithiasis—The Diagnosis of the Disease.

THE passage of a gall-stone along the biliary ducts excites several symptoms which, when they all occur in conjunction in the same patient, are pathognomonic of an attack of regular cholelithiasis. The presence of two or three of the most important of these symptoms is often quite sufficient to make an accurate diagnosis of the case easy, but in many instances they are improperly developed or they occur singly, and then, although the true nature of their cause may be suspected, it is often quite impossible to make a definite diagnosis of the case.

### The Symptoms of Regular or Uncomplicated Cholelithiasis.

The following are the symptoms which are met with in typical uncomplicated attacks of gall-stones:—

Pain or biliary colic ; increased temperature developing at times into a rigor ; jaundice, absence of bile from the stools (clay-coloured stools) ; constipation, or sometimes diarrhœa ; increase of bile pigments in the urine ; enlargement and sensitiveness of the liver, distension of the gall-bladder ; vomiting and derangements of digestion ; itching of the skin ; retardation of the pulse-rate ; hiccough in protracted cases ; nervous symptoms such as collapse, muscular convulsions, and emotional disturbances ; and pulmonary symptoms.

In the most typical cases all the above symptoms may be present during the illness, but more often some are absent, or but very incompletely developed.

A good deal of attention must be paid to most of these symptoms, so it will be well to consider each separately.

#### Pain, or Biliary Colic.

Pain, or biliary colic, is in many ways the most important of the above symptoms. It varies very much in character and severity in different cases, in some being so slight that it might not attract attention were it not for the appearance of other symptoms of gall-stones, whilst in others it is severe enough to cause general convulsions, loss of consciousness, serious collapse, with cold clammy sweats and feeble pulse, or even, in rare instances, sudden death. As a

rule, however, the pain is not bad enough to cause these serious results, but in the majority of cases the patients describe it as being so unbearable or agonising in character as to cause them involuntarily to "double up." It generally comes on suddenly, striking a patient of the labouring classes whilst he is at his work. Some observers state that the first attacks of pain come on at night whilst the patient is lying in bed. In one of my cases it caused most trouble about five or six o'clock in the morning. In patients who are subject to frequent attacks, the colic comes on from one to three hours after a meal.

*Character of the Pain.*—Different patients have described the pain as being of a dull, aching, tearing, pulling, boring, shooting, stabbing, burning, colicky character, and women have likened it to labour pains, but of a worse and more unbearable nature at times than the latter. Some will be unable to describe the character of the pain, but illustrate the sensation conveyed by it to their minds, by clenching their fists tightly and working the fingers in strong flexion, and other patients will describe it as being "like some one pulling their insides out of them." Budd laid great stress on the importance of a feeling of constriction round the lower part of the chest as a diagnostic sign of a stoppage of the common bile-duct generally caused by a gall-stone.

While the attack of colic lasts, the patient cannot bear the slightest pressure over the region of the gall-bladder, and generally lies on his left side with his knees drawn up to relax the abdominal muscles. They not uncommonly find the most relief by rolling

themselves into a ball with both legs well flexed against the abdomen.

*Situation of the Pain.*—As a rule the pain is most severe over the region of the gall-bladder, and between this and the epigastrium, but it may be felt in almost any part of the abdomen, and it is frequently referred to the chest and to the back, between and just below the shoulder-blades, or even in the lumbar region. In one of my cases the seat of maximum intensity of the pain was in the left hypochondrium and left shoulder, the right side being free from it. Similar cases have also been seen by other observers. Sometimes the pain is in the right breast, or may simulate intercostal neuralgia. Patients often tell you that the pain which commences in the epigastrium, right or left hypochondrium, seems to them to strike right through the middle of the back to just below the shoulders, others feel it more in the right shoulder; but Naunyn thinks that the pain is more often referred to this latter situation in hepatic abscess than in biliary colic. In one of Lauder Brunton's\* cases the patient complained of pain in the right iliac region, which came on in paroxysms and passed towards the umbilicus. It was supposed to be renal in origin. There was never any jaundice. The woman died eventually, and the gall-bladder was found to be full of calculi. Sometimes the pains radiate into the neck or head, into the right arm, even causing tingling sensations in the finger-tips, and into the right leg. Budd had a case in which the passage of calculi was always accompanied by pain

\* 'Brit. Med. Journ.,' Feb. 1st, 1896.

in the loins and the secretion of a large amount of urine.

The *Duration* of the pain varies very much. As a rule it lasts from one to three hours, and then ceases suddenly or passes off gradually. At times, however, the pain persists in all its severity for several hours, or in rare cases for a couple of days. One case is recorded by Naunyn\* in which with slight intermissions the pain persisted for five days.

Occasionally the cessation of the pain has been so abrupt that the patients either imagined they felt, or actually did feel, something "give way" inside them over the region of the duodenum. This sensation was due probably to the sudden escape of the calculus into the intestine.

Complete cessation of the pain is generally caused by the calculus escaping into the duodenum, but it may also follow upon the falling back, into the fundus, of a stone which has attempted to pass from the gall-bladder through the cystic duct. In one case which I saw the cessation of the pain was due to a small calculus, which was trying to pass through the duodenal orifice of the common duct, falling back into the wider lumen of the duct, in which there was room for it to lie without causing much obstruction.

The passage of a single calculus, or of several, may take place during the attack of colic. In the cases of shorter duration, and in the majority of all the cases, the passage of a single stone causes the colic, but in those which last longer, several calculi may pass out one after another. Thus, in the case of

\* Op. cit.

Naunyn's, which lasted five days, 214 calculi, varying from the size of small peas to that of cherry-stones, were passed by the bowel. Cases in which several stones are passed in the same stool are of frequent occurrence.

*Causes of Biliary Colic.*—The pain is chiefly caused, in all probability, by the spasm of the muscle fibres in the wall of the biliary passages, and this is added to by the forcible stretching of the duct wall by the passage of a large calculus. It has at times been stated that the pain of biliary colic may be caused by spasm of the rectus abdominis muscle; but this muscle is frequently in a non-spasmodic condition even during severe attacks of colic.

Some authorities consider that biliary colic may be excited by simple spasmodic contraction of the gall-bladder and bile-ducts set up by emotional causes, and quite irrespective of the presence of biliary calculi. Lépine\* is of this opinion, and thinks that hepatic colic may occur in hysterical women as the result of emotional disturbances. He also considers that the ingestion of certain articles of food is followed sometimes by "functional" hepatic colic. He made a *post-mortem* on a case which he considers supports his contention; but, although no calculi were found in the biliary ducts, there were a few grains of biliary concretion present, and the duct walls were in a contracted condition. Such a case can hardly be looked upon as one of hepatic colic set up by the emotions, for the biliary sand was sufficient to cause the colic.

\* 'Med. News,' 1894, vol. ii, p. 549.

Riedel\* believes that many cases of biliary colic occur in which no stone is present in the large ducts. The pain is then excited by the obstruction to the escape of bile by an inflammatory swelling of the mucous membrane of the ducts, which frequently starts from the gall-bladder. In operating on cases of biliary colic, he has found the gall-bladder full of granulation tissue, with the cystic duct obliterated, and no calculi in the common or hepatic duct, whilst in others on which he operated immediately after an attack of colic, the gall-bladder contained one large stone lying loosely in its cavity, the removal of which was followed next day by the escape of bile through the fistulous opening, a proof that the cystic duct was obstructed by swelling of its wall only, and not by an impacted stone. From these and other similar cases Riedel comes to the conclusion that biliary colic is frequently (in eleven out of seventeen cases) not due to a stone impacted in the large ducts, but probably to inflammatory swelling of the mucous membrane of the wall of the duct which leads to obliteration of its lumen. This inflammation frequently extends from the gall-bladder, where it is excited by the presence of calculi or by other causes.

*The Severity of the Pain is no Indication of the Severity of the Case*, nor of the size of the calculus which is endeavouring to escape into the bowel. Small, pea-sized, smooth stones frequently cause much more trouble than do larger or more irregular ones, and the expulsion of soft pasty concretions and of the very fine biliary gravel sometimes causes severe

\* Ref. Gumprecht, 'Deutsch. med. Woch.,' 1895, No. 15.

colic. The presence of small, regular, pea-sized calculi in the bile passages excites reflex spasm of the muscle fibres in the walls of the ducts, which is often of a more severe character than that caused by larger stones, for in the latter case the great size of the irritating body causes stretching of the muscle fibres, and almost entirely paralyses their ability to contract spasmodically.

The greater spasm of the biliary muscle induced by the smaller stone is to my mind comparable with the greater distress and trouble caused by a few hard scybalous masses in the rectum, compared with the discomfort felt when the rectum is loaded with hard faecal accumulations.

Large biliary calculi of the size of hazel-nuts, walnuts, pigeons' eggs, &c., are at times passed in the stools without the patient having suffered from biliary colic, or even from any symptoms severe enough to attract attention. Such concretions have escaped from the biliary passages by a slow process of adhesion of these structures to, and consequent ulceration through, the wall of a neighbouring portion of the alimentary tract. This process will be referred to later, under the complications of the disease. The painless escape from the body of very large gallstones has for a long time attracted the attention of observers, and the comparison of such an event with the agonising colic frequently caused by a small stone has given rise to the paradox—the larger the stone the less the pain.

### **The Causes which Excite an Attack of Biliary Colic.**

The onset of an attack of biliary colic is attributed to various causes, but especially to the reflex contraction which takes place in the muscle in the wall of the bile-ducts, as a result of the acid chyme entering the duodenum from the stomach. This contraction aids in the normal expulsion of the bile for digestive purposes, and generally takes place about two to three hours after a meal.

Calculi in the gall-bladder are very liable at this time to be dislodged from their resting position by the contraction of the walls of the viscus, and forced into the neck of the bladder or cystic duct, when they set up the obstruction and spasm of the muscle fibres which call forth the colicky pains.

Sudden or unusually forcible general muscular exertion—especially of the abdominal muscles—is not an uncommon means of dislodging a hitherto latent calculus. I have noticed that the patients frequently are attacked suddenly whilst stooping or bending down at their work, a position in which there is an increase of the intra-abdominal pressure, which acts especially on a large organ like the liver. The pressure on the liver tends to express the fluid contents of the biliary passages, and also to move a solid body in them. The older writers were very strongly convinced that violent passions frequently were the exciting cause of an attack of colic, the general muscular exertion induced by the gesticulations incident to their free display presumably causing an increase of pressure in the biliary passages, and dislodging any calculus

in them. It is also possible that the general emotional condition of the violent passion may cause an increased contraction of the muscle fibres in the wall of the gall-bladder or bile-ducts, and so dislodge a stone which resisted normal attempts to move it.

Direct violence applied over the region of the gall-bladder has been stated to have set up an attack of colic, and patients themselves frequently attribute the onset of their first attack to a strain or over-exertion.

In female patients subject to biliary colic, menstruation, pregnancy, and parturition are probably exciting causes of attacks. Cyr\* has met with several cases of this nature, biliary colic coming on in thirty-six instances very soon after parturition at full time, and in four others after abortion. Naunyn† mentions the case of a girl aged eighteen, who suffered from attacks of biliary colic which were coincident with the onset of menstruation. It is quite conceivable that the increased intra-abdominal pressure which accompanies the pregnant and parturient conditions, and the growth of abnormal abdominal tumours, may dislodge a gall-stone, and set it off on its attempted passage of the ducts. Errors of eating and drinking have from the first recognition of the disease been looked upon as causes, not only predisposing to the formation of the calculi but also exciting their movements, and the consequent biliary colic.

De Gruyther‡ made a *post-mortem* on a fatal case

\* 'Traité de l'Affection Calculeuse du Foie,' 1884.

† Op. cit., p. 55.

‡ 'Lancet,' Feb. 2nd, 1889.

of acute peritonitis, which had been ushered in by severe vomiting, set up by a heavy supper of pork. He found the gall-bladder ruptured, and it contained two probably latent calculi.

When the pain persists in a dull, aching manner for some time, it may be increased in its severity when the patient gets warm in bed.

### **Impaction of Gall-stones in the Biliary Passages.**

We have considered on a previous page how a calculus above a certain size, in endeavouring to escape from the bile-ducts or gall-bladder, meets with resistance from the walls of the duct and the ostium duodenale of the common bile-duct, through which it must pass before it can reach the intestinal tract. This resistance may be passive, as when a large stone is forced along the duct, and simply stretches the wall of the latter as it passes; or a more active opposition may be excited through the irritation of the mucous membrane by the stone, which causes contraction or spasm of the muscle fibres in the wall of the duct. The muscular spasm results in a narrowing of the lumen of the duct, the wall of which then seizes the stone and impedes its progress.

The migrating calculus may eventually overcome the forces which resist its escape, and pass out into the duodenum, or else, as frequently happens, it may be unable to force the passage of the ducts, and it then becomes fixed or impacted in some portion of the biliary system.

The impaction of a gall-stone in the bile-ducts may last a longer or a shorter time. If it persists,

the patient's condition becomes serious, and the case no longer remains of a simple nature, but complications ensue which may endanger the life of the patient. This latter condition will be referred to again later on.

The impaction of a biliary calculus most frequently takes place at the duodenal end of the common duct, where the narrow duodenal orifice of the duct offers great resistance to the passage of a stone. The cystic duct is the next most frequent seat of impaction, and then the neck of the gall-bladder, or where the latter joins the cystic duct. A calculus escaping from the gall-bladder will cause severe colic whilst it is passing through the cystic duct, which is greatly diminished when it reaches the wider common duct, along which it may pass without any difficulty. When the concretion reaches the ostium duodenale the pain returns with greater severity than ever.

In the ducts themselves the obstruction is generally complete, and persists until relief is finally obtained, whereas a calculus in the neck of the gall-bladder frequently acts as a ball-valve, being impacted for a time and then falling back into the body of the gall-bladder with relief to the obstruction. I have, however, also seen a very good example of a small concretion which acted as a ball-valve at the orifice of the common duct, and which caused temporary obstruction and typical biliary colic attacks, followed by relief to the symptoms and temporary recovery, due to the disengagement of the stone from the orifice of the duct.

The most serious results, as a rule, follow when

the stone is impacted in the common duct, for obstruction in such a situation prevents the escape of any bile into the intestine.

### The Escape of Gall-stones into the Intestines.

Following up the course of an uncomplicated attack of gall-stones, we find that the concretion eventually escapes into the intestinal cavity. Such an event may take place without the stone having become impacted in the biliary system, or it may only happen after there has been a complete obstruction to the escape of bile for a varying period of time. The final expulsion of the stone is brought about by the expulsive forces overcoming the obstructive forces, generally by causing a simple dilation of the passage sufficient to allow the stone to pass. The stone may also work its way in time through the ostium duodenale of the common duct by erosion of the tissues surrounding the orifice, and without exciting any complications of importance. But this latter process may cause serious symptoms which will be referred to under the consideration of irregular cholelithiasis. The stones once in the intestinal cavity tend to leave the body with the faecal matter, but very occasionally they may be vomited up.

More than half the battle is over when a calculus has entered the intestine, for unless it is of very unusual size it will pass out *per rectum* with, as a rule, no difficulty. Calculi as large as walnuts or pigeons' eggs are very commonly passed out by the bowel, and sometimes without any symptoms but slight uneasiness having previously troubled the patient.

Indeed, at times the difficulty and pain experienced in their attempts to pass the anus first attract attention, and the surgeon examining with his finger is surprised to find a large gall-stone in the rectum.

*Gall-stones found in the Fæces.*—Smaller stones, varying from the size of millet-seeds to that of hazelnuts, are frequently found in the stools of patients after attacks of biliary colic; but, on the other hand, it often happens that the most careful and thorough search made by experienced people fails to find a stone, even after the most typical and undoubted attacks of biliary colic. The reason for such a failure is either that the calculus has not left the biliary passages, or because many calculi, especially the softer, crumbly, amorphous forms, are completely broken up in their passage through the intestines. Naunyn proved this experimentally in man. He gave a man on three separate occasions five to seven gall-stones of various shapes and constitution, and about the size of peas, to swallow. The fæces were very carefully examined, and as a result, only three of the calculi were recovered. These were stones coated with a firm shell of pure cholesterin. The others which vanished were mixed bilirubin-calcium stones, and stratified gall-bladder stones which had no firm outer coat of cholesterin.

The search for gall-stones in the fæces is not a pleasant occupation, but its objectionableness is reduced to a minimum by use of the following method:—The fæces are placed on a fine hair or metal sieve, and then put under a tap, so that a stream of water of varying force can fall over them. An occa-

sional stirring or breaking up of the fæcal mass with a stick aids the washing away of the finer matter very much. Eventually there remains in the sieve only the coarser portion of the fæces, consisting chiefly of fragments of food which have been too large to escape through the fine meshwork, and all foreign bodies which may have passed along the intestinal tract. In this way any gall-stones which have escaped destruction in the intestines and have passed out of the body will be found, but the doctor himself ought to search for them, as an inexperienced person will pick out bodies which are not gall-stones and overlook those which are.

It is very common to mistake small masses of bile-stained fat, and soaps which are formed in the intestines, especially after the administration of large doses of oil, for gall-stones. A little care on the part of the physician will soon obviate this source of error.

The evil consequences likely to arise from the presence of gall-stones in the intestinal tract will be referred to later on.

**Jaundice** or **Icterus** is that discoloration of the tissues, most noticeably of the skin and conjunctivæ, which results from the deposition in them of bile pigments, which have been absorbed from the biliary passages by the lymphatic vessels in conditions in which there is obstruction to the escape of bile from the liver into the duodenum. The discoloration varies in tint from a pale straw-yellow to a deep olive-green or brown. The lighter shades can only be recognised in the eye, where they may be confused

with the condition of "pinguicula," in which there is a yellowish discoloration of the conjunctival tissues, usually of an irregularly triangular shape, especially on the inner, but also on the outer side of the cornea. Pinguicula is met with in adults chiefly, and is due to some chronic irritation. The discoloration of the conjunctiva from bile pigments is generally evenly distributed over the whole membrane, and not collected into two triangular patches. The faint yellow tints of jaundice cannot be recognised by gas-light. Bile pigments also appear in jaundice in the urine, sweat, milk, and serous exudations. The mucous membrane of the mouth may also be distinctly discoloured.

*Causes of Jaundice.*—As a rule, jaundice appears in cholelithiasis when the common bile-duct is obstructed by a gall-stone; but it may also occur in this disease when no calculus is present in the ducts. Riedel\* is strongly of the opinion that jaundice is not infrequently present when there is no stone in either the common or hepatic duct. He bases his conclusions on the conditions which he has found during operations on the gall-bladder, and states that the obstruction which causes the biliary stagnation is often due to an inflammatory swelling of the mucous membrane of the biliary passages which commences in the gall-bladder, whence it extends along the cystic and common ducts, obliterating their lumen. Colic, jaundice, and enlargement of the gall-bladder may result from this inflammatory obstruction of the large bile-ducts. He states that about two-fifths of the

\* Ref. Gumprecht, 'Deutsch. med. Woch.,' 1895, No. 15.

cases of jaundice in cholelithiasis arise in this way. He has found large, single stones in the gall-bladders of patients who have suffered from transitory attacks of jaundice, which could not possibly have entered the cystic duct, and when no other calculi were present in the ducts. In one case, jaundice occurred when the calculi were in a perforation abscess-cavity outside the biliary passages; and in others a small stone has been found in a widely-dilated duct, past which bile could easily escape. On the other hand, large calculi are met with obstructing the orifice of the common duct, and yet no jaundice appears. From the above facts Riedel considers that jaundice may arise from mechanical obstruction of the common or hepatic duct through the impaction of a large calculus in it, or else from an inflammatory swelling of the mucous membrane of the biliary passages, which is often set up by the irritation of smaller calculi in their lumen, or by extension from a focus of irritation in, or connected with, the gall-bladder.

In addition to the above causes, which act as obstructions within the lumen of the common bile-duct, the flow of bile along this passage may be impeded by the pressure exerted by a distended gall-bladder being pushed on to its outer wall. In a case of Terrier's,\* calculi in the cystic duct and gall-bladder caused an obstruction, either by such external pressure, or else by exciting inflammation of the mucous membrane, as in Riedel's cases. Terrier performed cholecystotomy on his patient, and bile reappeared in the stools on the eleventh day after the operation.

\* 'Acad. de Méd.,' Sept. 30th, 1890.

Liebermeister\* considers that jaundice may arise from disturbances in the activity of the liver cells in cholelithiasis. Normally a liver cell hands over the bile which it forms to the bile-ducts, and will not allow it to enter any other channel; but when the cells are in a pathological or moribund condition they cannot prevent some of the bile passing into the lymphatic vessels, and thence into the general circulation.

Pick\* and others suggest that purely nervous influences may act on the liver cells in such a way that the bile formed in them passes from them into an abnormal channel—namely, the lymphatic vessels, instead of into the bile-ducts. The irritation of a calculus in the biliary passages is sufficient to set up this perversion of the function of the hepatic cells. Biliary stagnation may be present at the same time; but Pick considers that it has nothing to do with the causation of jaundice.

Pick's theory is based upon Riedel's cases of jaundice, with no obstructing concretion; on the rapid development of an hepatic enlargement which takes place in cases of jaundice, and which he considers to be of nervous origin; and finally on the other symptoms of nervous origin—namely, colic, vomiting, cramps, and vaso-motor disturbances—which are met with in cholelithiasis. But whatever be the causes, the fact remains that jaundice is absent in many cases of biliary colic.

In Fürbringer's\* experience this is so only in the minority of the cases (25 per cent.). Naunyn, on

\* Ref. Gumprecht, 'Deutsch. med. Woch.,' 1895, No. 15.

the other hand, states that distinct jaundice is present in the minority of instances, and that slight jaundice is of only ambiguous signification, as it is met with in many abdominal affections, and is not at all diagnostic of biliary colic.

The discoloration is probably recognisable, even if only by a slight yellow tinge in the eyes, or by the presence of bile pigments in the urine, in about 75 per cent. of the cases of biliary colic. Its appearance is erratic even in different attacks in the same patient. Trousseau records a case in which a patient suffered for four years from frequent attacks of biliary colic before jaundice appeared. It may never develop even after repeated attacks of gall-stones. The time of the onset of the jaundice varies from one to several hours, frequently about twelve (Trousseau), after the appearance of the colic.

In one case the patient told me that he was seized with the pain in the first attack of gall-stones about 2 p.m., and that at 3 p.m. on the same afternoon, his fellow-workmen astonished him by saying that he had "the jaundice." He had been perfectly well previous to the attack. The patient noticed the discoloration himself very plainly when he went home in the evening.

Although jaundice is frequently caused by a calculus in the common or hepatic bile-ducts, it by no means happens that it is always present whenever gall-stones are lodged in these situations. Cruveilhier met with one case in which the common, hepatic, and large branches of the intra-hepatic bile-ducts were filled with innumerable calculi, and yet no jaundice ever ap-

peared, the bile being able to find its way in amongst the gall-stones, and between them and the wall of the ducts, and to escape into the duodenum. A much less extreme condition than this is frequently present, in which the bile is able to escape round even a large calculus which seems to completely block the lumen of the duct. Occasionally the jaundice appears for a time and disappears, to return again later on. This intermittence may be due to the escape of the obstructing concretion into the duodenum, followed shortly afterwards by the passage of another; but at times it is brought about by a stone which is endeavouring to escape through the orifice of the common duct, falling back into the wider lumen of the tube, and allowing the bile which has collected behind it to escape for a time. The stone then engages in the orifice of the duct again, and the jaundice reappears. Also when a large stone is obstructing the common duct the pressure which is generated behind it causes dilation of the duct immediately round the stone, thus making a passage along which the bile can escape into the duodenum.

*The Duration of the Jaundice* varies greatly according to the intensity of the discoloration, and this depends generally upon the length of time during which the stone remains impacted in the ducts. Even when the stone has escaped rapidly, and the jaundice has not been intense, it takes some days to clear up. With chronically impacted stones it may last for weeks or even years, but it frequently decreases or disappears for a time as the patient improves, to return again with another attack of colic. On the

other hand, when jaundice is due to obstruction of the common duct from cancer, it very rarely, if ever, entirely disappears or even improves.

*Clay-coloured Stools.*—Accompanying the appearance of jaundice is the absence of bile pigments from the stools, which results in their appearing pale, clay-coloured, or even at times almost white. An impacted stone which blocks the bile-duct and causes re-absorption of the bile, resulting in the pigmentation of the skin, will also prevent the escape of bile into the intestine; but sometimes the obstruction, though sufficient to cause the former condition, is not complete enough to prevent some bile from passing periodically into the intestine. In the latter condition the faeces will be bile-stained, and may remain so throughout the case. At other times a stone acts as a ball-valve, allowing the periodic escape of bile into the intestine after various lengths of time during which the obstruction has been complete. In such a case the stools are at times clay-coloured, and at others stained with bile pigments.

*The Action of the Bowels*, when there is complete obstruction to the flow of the bile into the intestine, varies in different cases. In some patients there is constipation, in others diarrhoea, whilst frequently the bowels act regularly every day. The clay-coloured motions are often of an intensely foetid odour, but they may be quite normal in this respect. Bile, therefore, is not essential as an intestinal antiseptic, nor as a stimulant for the normal peristaltic movements of the walls of the intestine.

In a case of Mayo Robson's in which a biliary

fistula persisted for fifteen months all the bile escaped externally, none entering the intestines, and yet the bowels acted regularly each day without any aperient being given, and the odour of the fæces was normal.

In Noël Paton's case of complete biliary fistula the fæces were always most offensive, but there was no diarrhœa, the bowels acting naturally as a rule, with only occasional help from an aperient.

In cases of biliary obstruction in which diarrhœa is a prominent symptom the bowels are often evacuated after every meal. I saw this condition cause a good deal of distress in a case of complete obstruction of the ostium duodenale of the common bile-duct from cancer of the head of the pancreas. The pathological condition of the latter organ may of course have had something to do with the diarrhœa, but a nurse of great experience told me that she had very frequently seen patients suffering from biliary obstruction uncomplicated with pancreatic affections in whom this evacuation of foul-smelling stools immediately after a meal was a troublesome symptom.

Constipation is also a common symptom in jaundice from gall-stones. It is hard to determine the cause of the constipation or of the diarrhœa, for either may be present in cases in which the intestinal conditions are apparently identical.

The presence of *bile pigments in the urine* is often the earliest indication of the onset of jaundice, and may be seen before even the conjunctivæ become discoloured. The tint of the urine containing bile pigments varies from a golden-yellow to an olive-

brown or green, and their presence can be recognised very readily by Gmelin's reaction.

### Itching.

Itching very frequently accompanies jaundice, and is at times extremely troublesome, keeping the patients awake at night and preventing rest during the day. It affects the whole of the skin, and the patients are often quite unable to restrain themselves from scratching the epidermis off, in the vain endeavour to obtain some relief.

Itching in jaundice is very difficult to treat medically, and it is, as a rule, only when the discoloration is improving that it passes off. It is often very severe when the jaundice is but slight, and frequently is entirely absent in marked discoloration of the skin.

### Gastric Symptoms.

*Vomiting* is a common symptom of attacks of biliary colic, and is often very troublesome. In those cases in which the pain has come on soon after a meal, the vomiting consists of a single emesis, which empties the stomach, and very frequently causes immediate alleviation of the colic; but in others, there is constant vomiting and retching although the stomach is empty, or only contains mucus and perhaps a little bile. This continued strain on the stomach exhausts the patient, and causes great tenderness in the epigastrium.

The presence of bile in the vomit is of importance, as showing that the biliary obstruction is not abso-

lute, and when it is met with, the stools generally contain biliary pigment.

In a few cases gall-stones themselves are found in the vomited matters, but probably only in complicated cholelithiasis, that is, when they have entered the stomach by the ulceration of a false passage between this organ and the biliary system. Some observers are of the opinion that all the gall-stones which are vomited during, and after, attacks of cholelithiasis have entered the stomach by such a false passage; but others believe that the smaller concretions at any rate, and bile can pass from the duodenum backwards through the pylorus into the stomach. Bile certainly can leave the duodenum in this latter way.

*Hæmatemesis* and *Melæna* occur now and then in the severer forms of cholelithiasis, but probably only in the irregular or complicated variety, and will be referred to fully when dealing with that form of the disease. The blood which is vomited or passed *per anum* is derived from the erosion of the mucous membrane of the stomach or duodenum which takes place during the formation of a fistulous communication between these organs and the biliary passages. Fatal results occur occasionally from the severity of the hæmorrhage.

*Derangements of Digestion.*—The digestion and absorption of all classes of foods except fats can go on perfectly well when no bile passes into the intestine, as is shown by the good health enjoyed by Mayo Robson's and Noël Paton's cases, in which all the bile escaped through a biliary fistula which discharged onto the surface of the abdominal wall.

But gastric disturbances are frequently present during, and after, acute attacks of biliary colic, the stomach being so intimately related to the liver that disturbances of the function of this latter organ are readily reflected in the former by the perversion of the normal gastric processes.

When jaundice is present, it is easily conceivable that the stomach should be affected by the amount of bile pigment and bile salts which are absorbed into the general circulation, and which cause general toxic symptoms; but as a rule, except in protracted and severe cases of jaundice, the patient does not suffer from digestive disturbances of a more serious nature than dyspeptic troubles. The latter condition may also be present in cholelithiasis when jaundice is absent; and it is probably of a bilious or hepatic nature, and due to the same morbid processes which determine the formation of gall-stones in gouty subjects.

### Enlargement of the Liver.

Enlargement of the liver is a very common accompaniment of attacks of biliary colic which have their origin in the presence of a calculus in the hepatic or common bile-ducts. It is probably present to a certain extent in all such cases in which the stone has remained impacted for even a few hours, but the enlargement in these transient attacks of biliary obstruction is too slight to be recognised clinically. When the condition has persisted for some hours or more, the hepatic swelling becomes more distinct, and can often be easily made out. In extreme cases

it may extend down into the right iliac region. The increase in size of the liver may be very marked when biliary colic is not a prominent symptom. It is then due probably to an infectious condition of the bile, which has given rise to a cholangitis or inflammation of the wall of the biliary passages. As a result of this latter condition the bile-ducts dilate, and the liver increases in size.

*Physical Signs.*—In many cases the enlarged liver is very tender and sensitive, and palpation of it is resisted by reflex contraction of the abdominal muscles; and it may also be spontaneously painful, and prevent the patient from moving about more than is absolutely necessary. This sensitiveness of the liver is often a prominent symptom early on in the case, especially when the bile is in an infectious condition. The pain of an enlarged liver in cholelithiasis probably arises from the stretching which the walls of the bile-ducts undergo as a result of their acute distension.

In contradistinction to this painful enlargement of the liver, it not uncommonly happens that the patient experiences no discomfort of any kind, even when a liver extending by enlargement downwards to below the umbilicus is palpated.

The enlargement of the liver may, of course, arise from obstruction to the outflow of bile from the common duct by other causes. In one case in which I saw a very marked hepatic enlargement, the obstruction was due to a carcinomatous growth involving the duodenal orifice of the duct, and causing complete retention of bile. The growth was not greater in area than that of a shilling, and was not more than

half an inch in thickness. The case originally was considered to be one of impacted gall-stone, but as the patient developed an acute pulmonary tuberculosis no surgical treatment was adopted. The liver was much enlarged, and was like a huge sponge; the bile-ducts were greatly dilated throughout the whole organ, and were filled with dark-green thick bile.

The slight enlargements of the liver are hard to palpate, but a quickly-drawn deep inspiration will frequently depress the liver so that its edge can be distinctly felt below the costal margin, the liver moving downwards normally with inspiration. A more marked increase in size can, as a rule, be easily made out by ordinary careful examination with the hand. There are, however, patients who have a normally rigid condition of the anterior abdominal muscles, which renders diagnosis by palpation almost impossible without the administration of an anæsthetic to overcome the rigidity.

When the enlargement of the liver is accompanied by tenderness, a reflex contraction of the abdominal muscles often develops as a protective measure, and this also increases the difficulty of diagnosing the condition of affairs. If palpation be impossible the presence of an hepatic enlargement may be made out by percussion, when the liver dulness will be found to extend to a varying distance below the costal margin.

In other patients the abdominal walls are so lax and thin that the edge of the liver can be grasped by the fingers, and the condition of the organ easily made out. In such cases pain or sensitiveness may

be present to a certain extent, but as a rule it is absent.

*Pathology of the Hepatic Enlargement.*—It seems difficult at first sight to explain the dilation of the bile-ducts which follows on obstruction of the common duct, in view of the fact that the pressure under which the bile is secreted is so low (24 mm. Hg.). Long-continued pressure, even if low, will eventually, however, dilate a vessel or tube which is not constructed for resisting strain. The periodic movements of the abdominal muscles and the respiratory movements of the diaphragm, both of which cause temporary but sudden rise of pressure in the biliary passages, will aid greatly in the stretching of the walls of the ducts. With the ducts dilated, the pressure of the contained fluid will be reduced for a time, during which a further formation of bile and secretion of mucus, &c., from the mucous membrane takes place, which adds to the quantity of fluid already present in the biliary passages.

The obstruction to the outflow of bile into the duodenum persisting, the increase of the fluid in the ducts prevents their walls from contracting, and provides the means by which the abdominal and respiratory movements can again raise the pressure in the biliary system and cause a further dilation of the ducts.

The large extra-hepatic ducts become widely dilated in some cases of long-continued biliary obstruction, and in some instances the distended hepatic and cystic ducts have been mistaken for an enlarged gall-bladder.\* The intra-hepatic ducts partake of the

\* Hermes. Ref. 'Brit. Med. Journ.' Epitome, Ap. 25th, 1896.

general distension, and give the liver the appearance, when cut, of a sponge. The gall-bladder, on the contrary, is only dilated in a very small minority of cases in which the obstruction to the escape of bile is due to the impaction of a stone in the common duct.

Around the dilated intra-hepatic ducts inflammation is set up, which leads to the formation of new fibrous tissue, and which is, in fact, of the nature of a true biliary cirrhosis.

The constant irritation of the wall of the bile-duct which is excited by the bile retained in it under pressure, is the probable cause of the development of the cirrhotic inflammation. Hamilton\* says that the fibrous tissue which develops around the dilated bile-ducts is composed of delicate and tortuous fibres which contain few, if any, nuclei, and which look very much like fine yellow elastic-tissue. Outside this finer, peculiar tissue the ordinary tissue of cirrhosis develops. The capsule of the liver is also thickened by the development in its deeper layers of the fine fibrous tissue.

The walls of the dilated extra-hepatic ducts are much thinned by the stretching to which they are subjected. Inflammatory thickening, even after long-continued distension, rarely develops.

### **Enlargement, by Distension, of the Gall-bladder.**

This is an important symptom in cholelithiasis, although only present in the minority of all cases of this disease.

\* 'Text-book of Pathology,' vol. ii, 1894.

*Causes.*—The distension of a gall-bladder generally results from the obstruction to the outflow of its contents which is caused by the impaction of a stone in the cystic duct or in its own neck, and rarely as a result of biliary obstruction due to a stone in the trunk or duodenal orifice of the common duct. I cannot call to mind one case in my own experience in which a stone in this latter situation has caused the distension of the gall-bladder, and, on the other hand, I have seen the condition induced by obstruction to the outflow of bile from malignant growths in several instances.

Courvoisier even believes that absence of dilatation of the gall-bladder in cases of obstruction of the common bile-duct is almost diagnostic of an impacted gall-stone in that situation, and, that when enlargement of the gall-bladder is present, the obstruction is in all probability due to other causes. This is quite contrary to the general belief.

The large extra-hepatic bile-ducts, and even the cystic duct, may be widely dilated, and yet the gall-bladder will be found to be normal in character.

It is very probable, however, that the gall-bladder is abnormally distended oftener than is believed to be the case in cholelithiasis, for when the liver enlarges and the lower edge moves down into the abdomen, even a great distension of the gall-bladder will be covered by the enlarged lobe of the liver and rendered impossible of palpation or of diagnosis.

The gall-bladder may be found to be enlarged when the liver is of its normal size. This happens when the obstruction is caused by a stone in the

cystic duct, which, while it will not allow bile to enter the gall-bladder, or the contents of the latter to leave it, does not interfere with the escape of bile from the common duct.

A gall-bladder which has its cystic duct blocked in the above way enlarges from the collection of the secretion of the mucous membrane of its own wall. It may also enlarge if a stone lodged in its neck act as a ball-valve, and only allow bile to flow past it in one direction, namely, into the cavity of the gall-bladder.

Another condition which acts as an obstruction to the cystic duct is the pressure on the latter by a distended gall-bladder itself. The cystic duct is curved like the letter S in its course between the neck of the gall-bladder and its junction with the hepatic duct, and pressure on it from a full gall-bladder, whether the fulness be caused by calculi or fluid only, will at times obliterate its lumen and induce further collection of the secretions of the wall of the gall-bladder, with consequent dilation of the latter.

Lastly, an inflammatory condition of the mucous membrane of the gall-bladder, frequently set up by cholelithiasis, may cause an adhesive inflammatory obstruction of the cystic duct and of the common bile-duct, which results in the dilation of the gall-bladder by the retention in it of the secretion of its own mucous membrane.

*The Physical Signs of a Distended Gall-bladder* are very distinct in many cases. The tumour generally assumes a more or less regular pyriform, or a more elongated sausage or banana shape, the fundus being

depressed downwards and inwards towards the umbilicus. Very often such an enlargement of the gall-bladder can be made out without any difficulty, but frequently there is a good deal of rigidity of the muscles of the anterior abdominal wall, similar to that described in connection with hepatic enlargement, and due either to natural causes or to a reflex contraction excited by a tender gall-bladder. Here again it may be necessary to relax the muscles by the administration of a general anæsthetic before the condition of affairs can be definitely determined.

On the other hand, with patients who have a thin and lax abdominal wall the tumour can be grasped by the fingers and its nature easily defined. Cases are, however, rare in which palpation is so easy, but, in patients with normal abdominal walls, an enlarged gall-bladder can often be easily examined with the hand.

In a straightforward case the swelling is immediately behind the anterior abdominal wall with no portion of the intestines intervening, and, when the tumour is of a moderate size, just outside the external margin of the right rectus muscle. The dilated gall-bladder will be felt to be of a pyriform or sausage shape, and to leave the shelter of the ribs about the level of the ninth or tenth costal cartilage. From this position the long axis of the tumour runs downwards and outwards, and the lower extremity frequently reaches, or even extends below, the umbilicus. When the stomach is distended, the tumour is frequently displaced outwards towards the right flank. The fundus of the dilated gall-bladder forms

the widest portion of the swelling when the latter assumes a pyriform shape, and from this broad, lower end the tumour narrows somewhat as it runs up towards the costal arch. Sometimes the distended gall-bladder has somewhat of a curve in it like a banana, but this condition can hardly be made out clinically.

In some cases, only the lower part of the tumour which appears in the abdomen can be made out, as an apparently isolated spherical body, near the umbilicus, that portion running up to the ribs being too deeply situated for palpation, or else lying behind the transverse colon, as happens occasionally.

The tumour moves downwards with inspiration, and upwards again with each expiration.

The swelling at times can be felt to be distinctly cystic, at others it is much harder and apparently solid, exploratory puncture with a syringe being the only means of deciding its true condition.

When filled by one or more calculi, a gall-bladder may be felt to be of stony hardness, and in very exceptional cases the calculi can be made to grate against each other, giving a sensation of dull crepitation. Enlargement with calcification of the gall-bladder wall takes place in rare cases.

The dependent or free portion of the tumour can often be displaced laterally, returning at once to its original position when allowed to. When examined bimanually with one hand placed over that portion of the anterior abdominal wall behind which the tumour lies, and the other posteriorly about two inches from the external border of the quadratus lumborum

muscle, the swelling may be grasped between the two hands, and be moved backwards and forwards.

In favourable cases the shape and extent of the tumour can be made out by the dulness which is obtained by gentle percussion over it. This dulness will then be found to be continuous with that of the lower margin of the liver, but sometimes when a portion of the colon crosses in front of the tumour there is a break between the dulness obtained over the fundus and over the lower margin of the liver, the resonant interval denoting the position of the bowel.

The distension of the gall-bladder is not uncommonly very great, reaching to below the umbilicus or even, as happened in cases in my own knowledge, down to the iliac region, when it simulates other cystic abdominal conditions of a hydatid, perityphlitic, or ovarian origin.

Terrier met with a case in which he removed twenty-four pints of gamboge-coloured fluid from a gall-bladder which had its cystic duct obliterated.

*Variations in the Size* of a distended gall-bladder are sometimes met with in cases in which there is a stone in the neck of the bladder which temporarily closes the cystic duct and obstructs the outflow of the gall-bladder contents. After the obstruction has lasted beyond a certain time, the calculus becomes disengaged from the orifice of the cystic duct, and the collection of fluid escapes from the gall-bladder. The condition returns again when the calculus re-enters the neck of the gall-bladder, and so on. A gall-bladder swelling may also appear and disappear during, and after, the passage of several calculi

through the cystic duct, and rare cases are recorded \* in which, after repeated attacks of biliary colic with the passage of calculi, the walls of the bile-ducts and gall-bladder get into an atonic condition, and the fluid collects, distending the gall-bladder. Pressure over such a tumour will cause a temporary diminution in its size.

When inflammation of the wall of the gall-bladder has accompanied the distension of this organ, it frequently leads to the exudation of lymph, which complicates matters by causing adhesions between this organ and the neighbouring viscera or abdominal wall. Inflammatory thickening also commonly develops, with a result that the enlarged gall-bladder loses its typical character, and becomes only a very irregular and almost indefinable swelling, with many of the diagnostic points alluded to above, especially the movement with respiration and the general mobility of the tumour, absent.

The *contents* of a distended gall-bladder vary according to the seat of the obstruction to their escape, and to the presence or absence of inflammation in the wall of the organ.

When the cystic duct is completely obstructed, the pigments contained in the bile which was in the gall-bladder at the onset of the obstruction become rapidly absorbed, and the fluid assumes a pale straw colour, and consists chiefly of the secretion of the mucous membrane. The fluid in such a condition contains mucin, often cholesterin, and more or less

\* Ref. Courvoisier, 'Casuistisch-Statistische Beiträge zur Pathologie und Chirurgie der Gallenwege,' 1890, p. 29.

albumen, pus, and red blood-cells if inflammation be present. The cholesterin may separate out in the crystalline form, in which case the fluid has a sparkling appearance. Micro-organisms are also frequently present. In not a few cases of protracted obstruction of the cystic duct the fluid in the gall-bladder is quite clear and colourless, and consists almost entirely of mucin. This condition is known as "hydrops cystidis felleæ" (q. v.).

When a calculus in the neck of the gall-bladder acts as a ball-valve and allows the entrance, but prevents the escape, of bile, the contents of the distended organ consist of a good deal of this latter fluid as well as of mucin, and are generally of a greenish colour. Bile is also present in a distended gall-bladder which results from obstruction in the common duct.

Gall-stones, either singly or in numbers, are also of course frequently found in the distended gall-bladder in cholelithiasis.

The number of pus cells present varies in different cases according to the severity of the inflammation of the wall of the biliary passages.

Several varieties of micro-organisms are found in the contents of distended gall-bladders, as mentioned in a previous chapter.

### Diagnosis of a Distended Gall-bladder.

The diagnosis of a distended gall-bladder must be made with care, for the physical signs and symptoms of such a condition are at times closely simulated by

those met with in abnormalities of certain other abdominal organs.

The pathological conditions from which it is especially hard to diagnose a distended gall-bladder are a floating or movable kidney on the right side, and an abnormal development of one of the lobes of the liver, which is met with at times in cases of cholelithiasis.

When the enlargement by distension of the gall-bladder is extreme, it may be mistaken for a perityphlitic abscess, or cystic conditions of the right ovary, right kidney, pancreas, and omentum. It will be necessary to consider these conditions separately.

*Movable or Floating Kidney.*—A movable kidney on the right side is not uncommonly mistaken for a dilated gall-bladder, and *vice versâ*. The former abnormal condition occurs most commonly in women—almost seven times as frequently as in men,—and the kidney on the right side is affected about thirteen times as often as the left kidney (Morris\*). A very good summary of the important points to be borne in mind when diagnosing between a dilated gall-bladder and a movable right kidney is given by Morris.\* I quote some of these points, and add a few others of importance.

1. The previous history of biliary symptoms.
2. The greater ease with which a distended gall-bladder can be felt as compared with a movable kidney, on palpating the abdomen from the front.
3. Variations in the size of the tumour must be

\* 'Brit. Med. Journ.,' Feb. 2nd, 1895.

considered with great care, for the kidney may be in a hydronephrotic condition, when it increases or decreases in size with the escape or retention of the fluid, in the same way that a gall-bladder does when the quantity of its contents is controlled by a ball-valve calculus in the mouth of the cystic duct.

4. A gall-bladder containing many calculi, or one large one, feels much harder than a movable kidney; but the latter, except when it is in a hydronephrotic condition, is firmer than a gall-bladder which is distended with fluid only.

5. Though movable laterally, and upwards and downwards with respiration, a gall-bladder cannot be pushed or manipulated by the hand downwards towards the pelvis, nor can it be prevented from moving with respiration. A floating kidney can be moved in almost any direction; it descends with inspiration, and can be prevented from ascending during expiration, and it has a special tendency to slip or roll away from beneath the fingers. A kidney also has a tendency to spring back to the loin when handled, whereas a gall-bladder tends to come forward to the anterior abdominal wall when allowed to do so.

6. Percussion over a distended gall-bladder generally yields a dull note, whereas a more or less marked tympanitic sound is obtained over a kidney, as the colon normally lies in front of this latter organ.

7. If the colon be inflated with air, the kidney theoretically is pushed upwards and backwards and out of reach of palpation, whilst the gall-bladder is pushed forwards to the abdominal wall. Inflation of

the stomach ought to push a gall-bladder tumour to the right. In practice, however, these methods do not generally yield good results.

8. A distended gall-bladder is often very tender and painful when touched, whereas the palpation of a movable kidney generally causes a sensation of sickness to the patient.

9. When examining the tumour bimanually with one hand on the anterior abdominal wall over the swelling, and the other placed posteriorly, care must be taken to keep the latter well on to the edge of the quadratus lumborum muscle, when kidney tumours can be grasped and moved backwards and forwards between the hands. If the posterior hand be placed an inch or so away from the quadratus muscle towards the flank, gall-bladder tumours can be grasped and moved about.

10. By getting the patient to lie over on the left side, the tumour can often be palpated much more distinctly than in the supine position.

11. When there is no intervening bowel, an exploratory puncture with a fine aspirating needle may give definite results, but care must be taken in doing this, as local peritonitis is liable to be set up by the puncture.

12. When a kidney is freely movable and descends well into the abdomen, its typical shape may be made out by careful palpation, and its upper limit can often be distinctly felt to be quite unconnected with the liver, whereas the upper portion of a gall-bladder tumour can rarely be traced with any degree of certainty.

Osler\* met with a case in which a nodular tumour on the edge of the liver was mistaken for the fundus of the gall-bladder.

Carcinoma of the gall-bladder may sometimes simulate a simple distension, but the onset of emaciation and of a cachectic condition in three or four months, will help to clear up the diagnosis.

*Linguiform Process of the Liver.*—One condition which not infrequently obscures the diagnosis of a distended gall-bladder is the development, from the quadrate lobe of the liver, of a tongue-shaped process of liver substance, which appears below the edge of the ribs in the exact situation of the normal gall-bladder. Trousseau and Cruveilhier met with and described the outgrowth, and of modern writers, Riedel† in 1888 devoted a good deal of attention to it. All observers seem to agree that the condition is developed as a result of cholelithiasis, and that it disappears after the latter is relieved by operation. Riedel met with this “linguiform” process in six cases of cholelithiasis, and in four of these the gall-bladder was enlarged.

A very good example of this condition occurred in the practice of, and was recorded by, Dr. Hellier‡ of Leeds. I quote the case rather fully.

The patient was a woman, æt. 32, who complained of a tumour in the abdomen, which she had noticed for two years. The tumour was very easily felt through the abdominal walls. It was lying a little to the right of, and above, the navel, and was characterised by great

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\* ‘New York Med. Journ.,’ 1894.

† ‘Berl. klin. Woch.,’ 1888, No. 29.

‡ ‘Brit. Med. Journ.,’ 1895, vol. ii.

mobility and by a very solid feeling. Its lower end, which the fingers could grasp through the parietes, felt like the end of a kidney or spleen. The upper part of the tumour was smooth, and only tender when firmly squeezed. It was so mobile that it could be placed either at the right or the left of the navel, and when the patient lay on the left side the tumour fell over on that side, reaching nearly three inches beyond the navel. It seemed to be quite free from uterine or other pelvic attachment, but to have some attachment near the liver, and it moved with respiration, but its exact relation to the liver could not be made out. On percussion, the tumour gave a fairly clear note all over, which was due, as it subsequently appeared, to resonance transmitted through the rather thin solid layer from the subjacent intestine. The clinical history showed that six years before, she had had an attack of jaundice and colic, and that she had noticed the present swelling for two years, during which time she suffered from pain at the epigastrium and between the shoulders, some tendency to vomit, constipation alternating with diarrhoea, and a good deal of throbbing pain and uneasiness in the lungs, which had made her life very uncomfortable, although she often was free from pain for several consecutive days. She had lost flesh. No definite diagnosis was made until an exploratory operation was performed, when the swelling was found to consist of two parts: (1) a cystic portion, which was the enlarged and distended gall-bladder, a gall-stone being impacted in the cystic duct and clearly perceptible from the outside; and (2) a tongue-like process of liver substance projecting from the lower edge of the liver, adherent to, and overlapping the gall-bladder.

The process of liver substance seemed to spring from the apex of the quadrate lobe. Three ounces of slightly turbid limpid fluid and seven gall-stones were removed from the gall-bladder. Patient was discharged as cured five weeks after the operation. At that time no tumour could be felt.

*Perityphlitis*.—Extreme and rapidly arising distension of the gall-bladder may be mistaken at times for a perityphlitic abscess. Dr. Dreschfeld examined one case in which there was a distinctly cystic swelling down in the right iliac region, which presented many of the characteristics of a rapidly arising peri-

typhlitic abscess, but as he considered that it was possibly connected with the gall-bladder, he punctured the swelling with an exploring needle and obtained some bile-coloured fluid which made the diagnosis of the latter condition certain.

Other observers have met with similar cases. A point which is useful in diagnosing between the two conditions is, that in perityphlitic abscesses there is pain on micturition, which is not present with an enlarged gall-bladder. Naunyn\* also considers that the presence of indican in increased amount in the urine is of diagnostic value, for he has always found it increased in cases of recent perityphlitis, and rarely so in gall-bladder affections.

*Ovarian, Renal, Pancreatic and Omental Cysts.*—Cystic conditions of the right ovary are not often likely to be confounded with a dilated gall-bladder, but I remember one case in which it was absolutely impossible, even with the aid of a vaginal examination, to say whether a cystic tumour of the abdomen was connected with the ovary or gall-bladder. The difficulty in diagnosing between these two conditions generally arises when the dulness over the cystic tumour is continuous with that of the liver and does not extend down into the iliac region. An exploratory laparotomy is, in such cases, advisable, and in the case I mention above was carried out, when the tumour was found to be an ovarian cyst.

Hydronephrotic conditions of the right kidney rarely cause such diagnostic trouble. Cysts of the pancreas and omentum are likely to be mistaken for

\* Op. cit., p. 86.

distended gall-bladders when there is no line of demarcation between the tumour and the liver, and the other physical signs are obscure. Both these latter conditions are very rare, but I have heard of their causing diagnostic trouble. They must be remembered as possible sources of error in the diagnosis of gall-bladder enlargements.

### The Temperature in Regular Cholelithiasis.

A rise of the patient's temperature very commonly accompanies an attack of biliary colic, the thermometer registering 103° or more. The pyrexia may be of a simple nature, or else it may occur in the form of a typical rigor. Coe\* (1757) considered that the occurrence of a fever with attacks of gall-stones was an accident, but Pemberton, † in 1820, recognised the true relation between the two, and noticed the presence of rigors. Budd, ‡ in 1845, likened the latter to the rigors caused by the presence of a stone in the urinary bladder, or by the passage of a catheter along the urethra, and it is quite possible that the biliary fever is a reflex pyrexia set up by irritation of the mucous membrane by the stone. Charcot§ considers that the pyrexia may be due to the absorption into the blood of toxic bodies formed by the micro-organisms frequently present in the bile in cases of cholelithiasis. The absorption may take place through tears or scratches made on the mucous membrane by a calculus passing along the biliary

\* Op. cit.

† 'Diseases of the Abdominal Viscera,' 4th ed.

‡ Op. cit.

§ Op. cit.

passages, or as a result of the high pressure developed behind an impacted stone.

Pyrexia does not accompany every attack of biliary colic. Fürbringer \* met with it in twenty-four out of forty-one typical cases of gall-stones.

As a rule the rise of temperature follows on the onset of the attack of colic ; but Naunyn has seen it precede the pain.

With the attack of colic over, the temperature quickly falls to normal ; but so long as a concretion remains in the biliary system, the patient is liable to the recurrence of simple pyrexial attacks, or of rigors, which are generally set up by, and accompany, the movements of a stone. The rigors return in some cases with a daily ague-like regularity which is very deceptive, especially when jaundice is absent. Instances have been known in which this has gone on for months before the development of jaundice enables the physician to diagnose the nature of the illness with certainty.

Cyr † saw one case in which, between four and five o'clock in the afternoon of every second day, an attack of biliary colic came on which commenced with pain in the epigastric and right hypochondriac regions, followed by shivering and marked pyrexia. The attack lasted from three to five hours. Slight jaundice appeared at the end of each attack, and simplified the diagnosis.

Chauffart ‡ states that the intermittent pyrexia of

\* 'X Cong. für inner. Med.,' Wiesbaden, 1891.

†\_Op. cit.

‡ Op. cit.

cholelithiasis is generally met with in old patients, and especially in females after the menopause. The exacerbations come on in the evening or at night. There is no splenic hypertrophy, no parasites in the blood, and the illness and fever resist the action of quinine, whilst they yield to the regular treatment of biliary colic. The irregular access of pyrexia in old people with healthy urinary organs ought to make one very suspicious of the presence of gall-stones. It may be the only symptom of cholelithiasis in the aged.

In the ordinary elevations of temperature in cholelithiasis the pulse-rate is very frequently not increased—in fact, it may be retarded; but when rigors occur it generally increases in rapidity according to their severity.

The pyrexia accompanying simple attacks of biliary colic must be distinguished from the febrile condition which is not infrequently met with in cholelithiasis in prolonged obstruction of the common bile-duct due to impaction of a gall-stone, or inflammation of the walls of the biliary passages. Jaundice generally accompanies the pyrexia in these cases, which Charcot termed “intermittent hepatic fever” (see p. 176). The elevation of temperature in intermittent hepatic fever is of a remittent or intermittent type, and is much more persistent than that which accompanies biliary colic; and although gall-stones are sometimes present in these cases of intermittent hepatic fever, the pyrexia may be quite independent of their movements, or else be more marked when attacks of colic come on.

The pyrexia in these cases is probably due to absorption of infectious matter from the biliary passages, which affects the body generally, sometimes setting up ulcerative endocarditis, and frequently causing acute enlargement of the spleen. Charcot's "intermittent hepatic fever" resembles malaria, but it is much more irregular in its exacerbations than the latter, and quinine has no effect on it. The presence or absence of the malarial parasite, or of jaundice, will aid the diagnosis.

### Cardio-vascular Symptoms.

The condition of the pulse varies greatly in different cases of biliary colic, and at different times in the same case.

It generally follows its ordinary course in the rigors and pyrexial conditions, that is to say, it is quickened with an increased temperature, but the number of beats may not be increased; they may even be diminished during the pyrexia. At times, in severe cases, the patient is in a state of collapse, with imperfect cardiac contraction and an imperceptible pulse.

Charcot considered that this effect on the heart was due to irritation of fibres of the pneumogastric nerve, which caused a reflex slowing of the heart and a tendency to its arrest in diastole. Simanowski\* states that frequently repeated artificial stimulation of the gall-bladder in animals is followed by degeneration of the myocardium and dilatation of the cavities of the heart even when the animals are well nourished.

\* 'Zeit. f. klin. Med.,' vol. v, p. 501.

The effect of such irritation is transmitted through the sympathetic nerves.

Frequently the pulse becomes very slow—as few as 40 beats or less per minute—especially in those cases in which jaundice persists after the subsidence of the acute symptoms.

### **Pulmonary Symptoms.**

Symptoms \* indicating pathological conditions of the pulmonary organs are occasionally met with in cases of biliary colic.

The chief of these are a hard, dry, exhausting cough, known to older writers as the hepatic cough, for which no cause can be found on examining the patient; and congestion of the base of the right lung, which is accompanied by pyrexia, expectoration of a stringy sputum, and the presence of fine bubbles over the congested area. This latter condition is supposed to be of vaso-motor origin, being set up reflexly from the irritation of the mucous membrane of the biliary passages.

### **Nervous Symptoms.**

The effect of the attacks of biliary colic on the nervous system is often great. Patients frequently tell you that they were quite unconscious of what they were doing during the pain. Local or general convulsions are occasionally set up, and hysterical attacks frequently occur in neurotic women.

The syncope which is met with on rare occasions is probably due to reflex inhibition of the heart's

\* Charcot's '*Traité de Médecin*,' 1892, vol. iii.

action by irritation of the vagus fibres in the biliary passages.

### The Urine in Cholelithiasis.

The urine passed during the attack of biliary colic is generally abundant in quantity and pale in colour. If no jaundice develops, there is, as a rule, nothing abnormal to be noticed in the urine, but when this symptom follows upon the colic, some of the bile pigments absorbed from the biliary passages are excreted in the urine, colouring it in various shades of olive-green and olive-brown.

The urine occasionally contains traces of bile pigments after attacks of colic which have been too slight to cause any noticeable discoloration of the skin or sclerotics. The bile pigments or their derivatives in the urine are best detected by Gmelin's test. The most delicate way of using the test is to drop two or three drops of the urine onto a flat, clean piece of white porcelain, and then, into the middle of this small quantity of urine, to add one drop of nitric acid which contains nitrous acid. Where the acid and the bile join, a green coloration is obtained when bile pigments are present, due to the formation of biliverdin, and extending from the green ring is seen a play of colours varying from blue, to violet, red and yellow. These latter colours are the result of the further oxidation of the biliverdin into bilirubin and the less known bile pigment derivatives.

Another, and almost equally satisfactory method of applying the test is to run carefully a column of

about one inch of the urine into a test-tube, which already contains some of the above-mentioned impure nitric acid. Where the two fluids join, the play of colours is seen as on the porcelain plate.

Marechal's test is also delicate. To a large quantity of the suspected urine in a glass urine-vessel, add a few drops of tincture of iodine, and stir up with a glass rod, when the urine will turn to a greenish colour if any bile pigment be present.

Frerichs\* states that jaundiced urine occasionally does not exhibit Gmelin's reaction when first passed, but does so after exposure to air. And Gamgee† refers to cases of jaundice in which the urine, though dark, does not exhibit the reaction for bile pigments. This latter condition is probably due to the transformation in the urine of the normal biliary pigments into urobilin, which does not give Gmelin's reaction.

The bile salts are present also in jaundiced urine in varying quantity. The usual test for them is that known as Pettenkofer's reaction. To about an inch of the urine in a test-tube, add either some powdered cane sugar, or about half an inch of a syrup of the sugar, and shake well until a froth is obtained, then pour down the side of the test-tube held in a slanting position, a few drops of concentrated sulphuric acid. If bile salts be present a beautiful violet or purple colour will be seen in the froth.

It has been known for some time that the addition of a drop of a mineral acid or of acetic acid to urine

\* 'Klinik der Leberkrankheiten,' vol. i, p. 100.

† Op. cit., p. 366.

containing bile will often cause a slight but distinct, cloudy, white precipitate to form. Opinions as to the nature of the body which is thus thrown down differ. Some authorities consider that it is mucin or an albuminous body, whilst Grocco\* comes to the conclusion that the precipitate is composed of bile pigments.

Mayo Robson † is practically certain that the cloudy appearance is due to the precipitation of bile acids. I have frequently seen this precipitate form myself, and am of the same opinion as Mayo Robson, namely, that it is composed of bile acids, which are formed from the bile salts contained in the jaundiced urine, by the addition of the mineral or acetic acid. Bile salts are very soluble in water, whilst bile acids are all but insoluble, and the latter are formed and precipitated from a solution of the former in a test-tube by acidulation. I once precipitated twelve ounces of jaundiced urine containing the substance in question, filtered, and extracted the precipitate with ether, and then with absolute alcohol. The former will not dissolve bile acids, but the latter does readily. After treating the precipitate with absolute alcohol and filtering, I evaporated the filtrate to dryness, and with the residue was able to obtain a very distinct violet colour on the addition to it of a crystal of cane sugar and a drop of concentrated sulphuric acid, the mixing of the three substances being done on a white porcelain slab.

Albumen occurs occasionally in icteric urine, though its presence is not due to the jaundice itself,

\* Ref. 'Brit. Med. Journ.,' Aug. 22nd, 1891, Suppl. † Op. cit.

but, apart from coincident kidney affections, to the general debilitated condition into which some patients get as a result of long-continued jaundice.

In order to recognise albumen by tests, the urine must be acidulated with a few drops of acetic acid, and filtered to remove the precipitated bile acids. If the filtrate be boiled, albumen will then, if present, come down in the usual way.

Sugar is found occasionally, but whether its presence is a coincidence, or whether it is a result of the cholelithiasis, is hard to say.

Casts of the renal tubules, generally hyaline but occasionally epithelial in character, are commonly found in icteric urine. They are stained yellow by the pigment. Their pathological significance is not known. Cholesterin is never met with in the urine of jaundiced patients.

### Diagnosis of Attacks of Gall-stones.

The diagnosis of typical attacks of "gall-stones," with the sudden onset of severe pain in the right hypochondriac region, radiating to the epigastrium and shooting through to the back, accompanied by a rise of temperature, frequently by vomiting, and followed in the course of a few hours by jaundice, bilious urine, and if the case lasts long enough, by enlargement of the liver, distension of the gall-bladder, constipation and clay-coloured stools, is not difficult.

As a rule, the severer cases are easily recognised, and it is the milder forms which cause the most mistakes to be made.

There are many cases in which no distinct symptoms

appear, and in these it is almost impossible to make any diagnosis until the case has been watched for some time, or unless there is a definite and reliable history of previous similar attacks of biliary colic.

Patients may complain of nothing more than a sense of constant uneasiness in the region of the liver or stomach, with no definite pains and no true crisis, and this condition of affairs goes on for some time, when the onset of a typical attack of biliary colic clears up the case. Cyr thought that these irregular cases frequently developed about the change of life in women.

Severe pain, but in irregular situations, often obscures the diagnosis; thus, when in the epigastrium, stomach troubles are thought of, when in the lumbar region it is impossible for a time to eliminate renal colic, and pain in the right mammary region has suggested cancer of the breast or intercostal neuralgia, and in the abdomen, peritonitis and perityphlitis.

Budd pointed out the similarity between attacks of gastric pain excited by lumps of badly masticated food in the stomach, and biliary colic. The pain arising from a gastric ulcer is at times confused with that of biliary colic, but the former generally comes on almost immediately after food, and the latter not until two hours or more after a meal. There is more similarity between the usual time of onset of the pain which arises from a duodenal ulcer—namely, about two hours after a meal—and that of biliary colic. A previous history of hæmatemesis and the younger age of the patient is greatly in favour of a round ulcer of the stomach or duodenum.

In a case of dilated stomach in a man, which I saw, intensely severe pain in the epigastrium, which used to come on regularly in the evening, simulated biliary colic. The pain in this case resisted rather large doses of morphia, but was instantly relieved by the use of the stomach-tube, by means of which some intensely acid, pungent-smelling fluid was removed.

The pain of lead colic may closely resemble biliary colic, but the former is relieved, whilst the latter is intensified, by pressure on the abdomen. The other signs of plumbism, especially the blue line on the gums, will probably be present, and settle the diagnosis.

When considering pain in the lumbar region it must be remembered that nephrolithiasis and cholelithiasis are not uncommonly present in the same subject. The pain of biliary colic, whether it be felt in its normal situation over the gall-bladder or be referred to any of the above unusual positions, can generally be brought out by pressing over the gall-bladder. The patient then feels it where it has occurred before, and the true cause of the pain is rendered clearer.

In general peritonitis there is almost complete absence of the respiratory movements of the diaphragm and abdominal muscles, whilst in biliary colic the character of both these forms of respiration is very little altered from the normal, except in cases in which the liver and gall-bladder are very sensitive, when abdominal respiration is a good deal resisted.

In peritonitis the patient lies on his back with both legs drawn up towards the abdomen, whilst

during an attack of biliary colic, with tenderness of the liver and gall-bladder, most ease is secured by lying on the left side with the legs flexed on the abdomen.

The severity of accompanying symptoms, as for instance syncope, convulsions, hysteria, &c., not uncommonly masks the more essential signs of cholelithiasis. Regularly recurring rigors without distinct pain simulate malarial attacks, and cases in which biliary colic recurs regularly, but is the only symptom, are at times not suspected to be due to the passage of gall-stones.

In nearly all these irregular forms the diagnosis is, however, eventually settled by the development of a typical attack of gall-stones, followed often by the appearance of biliary concretions in the stools. The result of treatment is also often of great use in clearing up the diagnosis of obscure cases.

### **A Case of Biliary Obstruction from an Impacted Gall-stone.**

I will close this chapter on the symptoms of regular cholelithiasis with a short account of the clinical history of a case which was, in all probability, one of a gall-stone impacted in the common bile-duct. I am indebted to Dr. Steell for permission to refer to the case.

A man, æt. 42, married, and a boiler-maker by trade, was admitted into the Manchester Royal Infirmary on January 2nd, 1896. He had suffered from "gastric fever" twenty-one years ago, in consequence of which he had to lie in bed fourteen days, and was

away from work altogether three weeks. The exact nature of this illness cannot be definitely determined, as the patient's account of it was so vague. It was possibly, however, a mild form of enteric fever. Since the above illness he has remained well until thirteen weeks previous to admission into the hospital, when, whilst at work, he felt a sudden, severe pain in the region of the gall-bladder, striking through to his back a little below the right shoulder-blade. He had had his dinner at noon, and the pain seized him at 2 p.m. It was severe enough to "double him up," and lasted for a quarter of an hour, when he vomited his half-digested dinner and some bile. After the stomach was emptied, the pain became easier. He was able then to continue with his work, and at 3 p.m., one hour after the onset of the pain, his fellow-workmen astonished him by telling him that he had gone yellow. This he saw for himself, especially in his eyes, when he went home after work-time. The next morning he felt too sick to get up, and the pain was present then, as a dull, gnawing sensation, and has remained so since, increasing at times into severe paroxysms every two or three days, which lasted about three hours. He has remained in bed since the beginning of the illness. He "shivered awfully" twice at the onset of the attack, but does not seem to have had a true rigor. The jaundice became very marked, with clay-coloured stools but no marked constipation, and high-coloured urine, and very troublesome itching developed.

He always vomited during the attacks of pain, and felt much relief afterwards. He states that the vomit was as a rule brownish, with bile occasionally in it, or at times cocoa-coloured. He never found any gall-stones in the stools. He states that he lost 3 st. in fourteen weeks. He has been in the habit of taking a "moderate" amount of alcohol regularly.

Father died aged 48 from "inflammation of the bowels." Mother alive and very healthy. No similar case in the family. Brothers and sisters healthy.

#### *Condition on Admission into the Hospital.*

January 2nd.—On admission, patient was seen to be very much jaundiced and a good deal emaciated. He weighed 8 st. 8 lbs. The examination of the abdomen by palpation was difficult, as the epigastric and hypochondriac regions were tender to pressure. The liver dulness was, however, apparently increased in a downward direction to the extent of about one inch below the margin of the ribs,

but the edge of the organ could not be felt. No enlargement of the gall-bladder or spleen could be made out.

The urine was high coloured, and contained bile pigments, bile salts, and urates, but no albumen or sugar. The specific gravity was 1015.

January 3rd.—The temperature last evening was 100·6° F. (38·1° C.). During the night he vomited some bile-coloured fluid twice, and was troubled with the pain again. The temperature this morning is normal. Bowels opened twice; stools pale and almost clay-coloured; pulse 72.

5th.—Last evening the temperature rose to 103·2° F. (39·5° C.); no rigor. Complained of pain in the pit of the stomach yesterday, and to-day it can be brought on by palpation over the gall-bladder. No further vomiting; itching very troublesome.

7th.—Condition generally better; pain easier. The temperature has fallen gradually to normal. No further vomiting; pulse 60.

13th.—Improvement has continued; the pain has gone, the discoloration of the skin is much less, and there is only a trace of bile pigment in the urine. The itching is better.

From this date patient improved slowly but steadily, and was sent to the convalescent hospital on February 8th, 1896, when he weighed 9 st. 6 lbs. He remained there five weeks, during which time he increased 16 lbs. in weight; he had no return of the symptoms, and was discharged cured.

The only medicinal treatment adopted was one or two teaspoonfuls of Carlsbad salts administered in hot water in the morning to keep the bowels well opened.

This case is interesting, for although many of the typical symptoms of biliary obstruction from a stone in the common bile-duct were present, a diagnosis of the true nature of the obstruction could not be definitely made for some time. The history of the vomiting of cocoa-coloured fluid previous to admission rather complicated matters, for it could not be ascertained whether or not the coloration was due to blood. Assuming that hæmatemesis had really taken place before admission into the hospital,—no blood was vomited after the patient came under Dr. Steell's

care,—the case might have been one of malignant disease of the pylorus and duodenum involving and obstructing the orifice of the common bile-duct, or one in which a biliary-gastric or biliary-duodenal fistula was being formed by a stone in the common duct. There were no indications which pointed to the hæmatemesis being due to alcoholic cirrhosis of the liver or to a gastric ulcer. The points in favour of malignant disease were the great emaciation, the cachectic appearance of the patient, the constant burning pain in the epigastrium, the absence of any improvement in the patient's condition, and the persistence of the jaundice. When, however, improvement set in, the diagnosis of malignant disease was rendered very improbable, and the case assumed a more simple aspect. Still assuming that hæmatemesis had occurred, the most likely cause of it would be the formation of a fistulous passage between the common bile-duct and the stomach or duodenum. If no blood had been vomited, then all the symptoms, especially with the absence of distension of the gall-bladder, would be explained by the impaction of a stone in the common bile-duct or in its duodenal orifice.

The great improvement which took place during the last two months in which the case was under observation, distinctly points to the patient having suffered from an attack of gall-stones, but whether the gall-stone eventually escaped from the biliary passages, and if so, whether it was by means of a biliary fistula or *per vias naturales*, it is impossible to say.

## CHAPTER VIII.

Irregular or Complicated Cholelithiasis—Impaction of Gall-stones in the Biliary Passages—Diagnosis of the Seat of Impaction of a Biliary Calculus—Local and General Complications of Cholelithiasis—Chronic Jaundice—Infection of the Bile and its Consequences, Cholangitis, Cholecystitis and Hepatitis—Cholangitis—Cholecystitis and Empyema of the Gall-bladder—Calculous Hepatitis—Affections of the Portal Vein.

It has been shown in a previous chapter, that in regular or uncomplicated cholelithiasis the attacks of gall-stones end by the escape of the obstructing concretion from the biliary passages into the duodenum *per vias naturales*, after varying lengths of time, without any damage to the tissues resulting. From the intestinal tract the concretion passes out of the body, probably without exception, in the stools, and in very many instances without attracting attention.

This favorable termination happens in the majority (66 per cent.) of the cases of cholelithiasis, but unfortunately in a very large proportion of the patients the disease runs a more unfavorable course, and not uncommonly it ends fatally.

### Irregular or Complicated Cholelithiasis.

The first step towards the onset of an irregular or complicated case is provided either by the irritation of the wall of the gall-bladder, which frequently results from calculi in this organ, or by a gall-stone

which, in trying to escape into the duodenum, becomes impacted or fixed in one or other of the hepatic, cystic or common bile-ducts, or in the ostium duodenale of the last duct, and which completely, or almost completely, prevents the flow of bile past it. Biliary stagnation with its accompanying sources of danger is brought about by the latter event, and very often also by the former, through the inflammation arising in the gall-bladder, and extending along the mucous membrane of the cystic and common ducts and obliterating their lumen.

### The Impaction of Gall-stones in the Biliary Passages.

The impaction of a stone almost always takes place in the cystic or common duct, and the frequency with which either of these ducts is obstructed varies greatly.

Schröder\* found calculi equally often in both ducts (13 per cent. of *post-mortems* on 141 cases of gall-stones) in older subjects impacted, whilst Courvoisier\* only met with them in the common duct in 3·9 per cent., and in the cystic duct in 6·7 per cent. of his cases of gall-stone autopsies.

Calculi are only rarely found in the hepatic duct (1 per cent. of all cases of gall-stone autopsies), and more rarely still in the intra-hepatic ducts.

The majority of the calculi found in these ducts are larger in size than a cherry.

When in the common duct, the stone is impacted at the duodenal end, or in the ostium duodenale itself, in about half the cases.

\* Ref. Naunyn, op. cit., p. 88.

The greater number of all biliary calculi are developed in the gall-bladder and migrate into the large ducts after they have grown to a certain size. They may even pass back into the hepatic duct in this way. Occasionally stones formed in the intra-hepatic ducts pass along into the extra-hepatic ducts.

It has been stated in a previous chapter that gall-stones may increase in size after they have entered the large extra-hepatic ducts, provided, of course, that they remain for some time in the duct. Concretions also at times, but very rarely, arise *de novo* in the large ducts. A small stone which has passed into the common bile-duct may remain there for some time without causing obstruction, and then, having increased in size by the deposition of stone-forming material, it becomes too large to allow any bile to escape past it into the duodenum, and symptoms of complete biliary obstruction develop.

### Diagnosis of the Seat of Impaction of a Biliary Calculus.

There are certain differences in the physical signs and symptoms resulting from the obstruction of the different portions of the large extra-hepatic bile-ducts which it will be well to consider here.

*Cystic Duct.*—When the onset of the obstruction by a calculus in this duct is sudden, there is generally a rather rapid dilation of the gall-bladder, due probably to the exudation of inflammatory fluid in addition to the retention of the normal secretion of the mucous membrane. When, on the other hand, the closure of the duct is more gradual, inflammation of the wall of

the gall-bladder is set up at the origin of the cystic duct, which extends to the fundus and results in a shrinking and atrophy of the whole gall-bladder. This latter is by no means an uncommon occurrence in obstruction of the cystic duct from gall-stones.

Enlargement of the liver does not follow a simple obstruction of the cystic duct by a gall-stone.

*Hepatic Duct.*—When calculi are found in this duct they are generally present at the same time, or have been before, in the common duct.

*Common Duct.*—The results of the impaction of a stone in this duct are very important. Dilatation of the ducts behind it comes on to a varying extent, whilst on the duodenal side of the obstruction the duct generally contracts, or, in cases of long-standing, atrophies or becomes almost obliterated. The liver also is enlarged as a rule. The cystic duct is involved in the dilatation behind the impaction, and may enlarge so as to resemble, and be taken for, the gall-bladder, but the latter organ is rarely dilated when the obstruction in the common duct is due to a gall-stone. In the majority of cases it even atrophies. When, however, the obstruction is due to other causes, dilatation of the gall-bladder is the rule. Thus out of 109 cases of dilated gall-bladder from obstruction of the common duct, the obstruction was due to biliary calculi in seventeen instances only, and in the remainder to other causes—tumours, occlusion, &c. (Courvoisier).\*

The same writer also collected seventy-eight cases of atrophied gall-bladder which occurred in obstruction

\* Op. cit., p. 57.

of the common duct, and in which the cystic duct was patent, and in seventy of these the cause of the obstruction was an impacted gall-stone. In the remaining eight cases the obstruction was due to other causes, but in five of them the gall-bladder contained concretions which had evidently been the cause of its contraction.

When the gall-bladder does dilate in consequence of the impaction of a calculus in the common duct, the enlargement is not very marked.

The *symptoms* excited by a stone obstructing the cystic duct differ in one or two important respects from those caused by a similar obstruction in the common bile-duct. The pain is greater when a stone is passing through the cystic duct than when it is in the common duct, but less than when engaged in the ostium duodenale of the latter. A calculus in the common duct almost invariably causes the onset of jaundice and its consequences—itching, bilious urine, and clay-coloured stools; whilst obstruction of the cystic duct is not followed by jaundice except in those rare cases in which a gall-bladder, enlarged by the obstruction of this latter duct, or a cystic duct and gall-bladder containing calculi, presses on the common duct and obliterates its lumen.

#### Local and General Complications of Cholelithiasis.

The complications of the disease follow as a rule on the impaction of one or more gall-stones in the bile-ducts, or on their retention in the gall-bladder. The results of such impaction or retention of gall-stones are obstruction to the flow of bile and irritation

of the wall of the biliary passages. These latter conditions excite in their turn further complications, the nature of which varies according to the situation of the offending calculi. The most important of these complications are chronic jaundice, infection of the bile by micro-organisms, ulceration of the walls of the biliary passages, malignant disease of the walls of the biliary passages, interstitial pancreatitis, and cirrhosis of the liver. Each of these affections has sequelæ of its own. It will be best to consider each complication separately in the above order.

**Chronic Jaundice.**—Any of the causes of the transient jaundice which appears in attacks of biliary colic may easily, if unrelieved, lead to the development of chronic jaundice. This latter condition, however, appears most frequently as a result of the impaction of a calculus in the common bile-duct or in its duodenal orifice. The obstruction to the flow of bile in such cases is due to the mechanical resistance of a stone in the duct, and also to inflammatory thickening of the mucous membrane of the duct, which frequently results from the irritation of the retained calculi. As long as the conditions which cause the jaundice exist, the discoloration of the skin remains.

*The duration* of chronic jaundice varies greatly, from so many weeks to six years.

An interesting case of jaundice lasting six years, which resulted from the impaction of a gall-stone in the biliary passages, is recorded by Chadwick.\* The following is a brief account of the case.

\* 'Brit. Med. Journ.,' May 25th, 1895.

A married woman, æt. 36, was seized in January, 1889, with excruciating abdominal pain, which was accompanied by vomiting but by no rigor. Next morning jaundice was noticed, and it remained present until the patient's death in December, 1894.

No history of any subsequent or previous attack of similar pain was obtainable, and the patient remained in fairly good health until January, 1892, when she was admitted into the Leeds General Infirmary. At this time she was considerably jaundiced, the liver was enlarged, ascites was present, and there was considerable tenderness over the region of the gall-bladder. Xanthelasma was present, œdema of the legs appeared, albumen was found in the urine, and "hard nodules" were felt in the right lumbar region. The ascites diminished whilst the patient was in the hospital. The diagnosis of malignant disease of the liver was made. The woman left the hospital, and was readmitted in October, 1894. At this time she was markedly jaundiced, and looked aged. Examination revealed the presence of hæmorrhagic staining of the tissues, great enlargement of the spleen, irregular outline of the abdomen, visible peristalsis, dilatation of the stomach, but no ascites, no xanthelasma, and no enlargement of the liver or gall-bladder. Violent hæmatemesis and melæna ensued in spite of the administration of chloride of calcium. After this the splenic enlargement diminished, but the patient died three days later (December 3rd), or five years and eleven months after the primary onset of the jaundice.

A *post-mortem* examination of the case was made, when the following conditions were found.

There was general matting together of all the abdominal contents by old peritonitis. The spleen weighed 21 oz.; liver of normal size. The gall-bladder measured three-quarters of an inch in length and one third of an inch in breadth. No trace of a cystic duct could be found. On opening the duodenum a shallow depression lying half an inch from the pylorus was seen, from the bottom of which an aperture, about one eighth of an inch in diameter, led into a cavity in which an egg-shaped gall-stone weighing four grammes, when dry, was found. From the cavity in which the stone was lying a passage, one eighth of an inch in diameter and two inches in length, communicated with a distended hepatic duct seven inches long, leading to the left lobe of the liver. The bile papilla opened into the duodenum three inches from the pylorus, and the common duct appeared normal and pervious to fluid.

The description of this case is not as clear as one could wish, but it is probable that the stone left the gall-bladder and became impacted at the junction of the common and cystic ducts, then ulcerated through the wall of the duct, setting up general peritonitis, which subsided after a time. The stone probably escaped into a local peritoneal abscess outside the common duct, but communicating with the hepatic duct. In this situation the stone exerted obstructive pressure on the wall of the common bile-duct, and finally eroded a small hole through the duodenal wall, through which, however, it was unable to escape itself. The obstruction of the common duct was not complete, for although the jaundice existed for six years, the stools were not always clay-coloured.

An instance of recovery after jaundice had lasted nearly six years is recorded by Murchison,\* in Case cxxxii in his 'Clinical Lectures on Diseases of the Liver, &c.' During the time the jaundice was present, the patient suffered from frequent attacks of pain, with rigors, vomiting, high-coloured urine, clay-coloured stools, and diarrhoea. She was also much debilitated, but towards the end of six years the jaundice began to pass off and the general condition improved.

Both the above cases are of exceptionally long duration, but many others have been seen in which the jaundice lasted two or three years (two and a half years—Ramskill).†

As a rule, however, the case terminates one way

\* Third edit., 1885.

† 'Lancet,' 1876, i, p. 379.

or another in two or three months, and a case is recorded (Spencer)\* in which death occurred in the very short space of ten days.

The jaundice is not of necessity accompanied throughout its course by clay-coloured motions, for bile can frequently escape in small quantity past the obstructing stone, either between it and the wall of the duct, or else by a new channel. In Chadwick's case a small amount of bile always escaped past the obstructing stone, either through the patent common duct, or through a small opening into the duodenum which was not large enough to allow of the escape of the calculus. The stools are in many cases clay-coloured for a time, and then contain bile as described in a previous chapter.

As a rule, an attack of biliary colic precedes the appearance of jaundice, but sometimes the latter symptom develops without any previous pain. Thornton† met with one case in which icterus came on gradually without any pain and then suddenly became intense with accompanying loss of appetite and flesh. Several similar cases have from time to time been recorded.

Elevation of temperature may be absent throughout the course of the jaundice, as seems to have been the case in Chadwick's patient, or there may be attacks of pyrexia, indicating either the probable presence of biliary infection or simply the movements of calculi in the ducts.

*The Termination of Chronic Jaundice* is either in recovery after the escape of the stone by natural pro-

\* 'Brit. Med. Journ.,' 1879, i, p. 149.

† Ibid., February 1st, 1896.

cesses or after its removal by operation from the biliary passages, or else in death.

A fatal termination may result from the debilitated condition which is so liable to set in after jaundice has been present for a length of time. Patients, in whom jaundice persists, become cachectic from the continual absorption into the circulation of the biliary constituents, and their blood becomes impoverished, and often loses its power of coagulation to such an extent that it resembles the condition in which it is found in the hæmorrhagic diathesis. For this latter reason surgeons often object strongly to operate on cases in which jaundice has been a prominent symptom for more than a few weeks.

As a result of the changes in the blood, cholæmia comes on with its ever-increasing debility and final coma, and death is at times due to this cause.

*Xanthelasma* \* is not at all uncommonly met with in cases of long-standing jaundice (over eighteen months), though the exact processes which determine its development are not known. It was present in Chadwick's and Murchison's cases of chronic jaundice.

*The Diagnosis between Cholelithiasis and New Growths* as the cause of chronic jaundice is at times difficult.

In cholelithiasis there is generally a history of previous attacks of colic, the pain is paroxysmal, the jaundice often improves, or may even vanish completely for a time, and the stools frequently are highly-coloured with bile, and then clay-coloured,

\* 'Trans. Path. Soc. Lond.,' 1882, p. 381.

pyrexia is common, the liver and spleen are often enlarged, no nodules or evidences of new growths can be felt over the liver or gall-bladder, and the general condition of the patient is not so low and serious as in obstruction from malignant growths.

When the jaundice is due to obstruction from carcinomatous growths the patient rarely lives more than twelve months after its onset, and the discoloration never passes off, the pain is often very persistent, the stools remain pale, the liver frequently is enlarged and nodular, the gall-bladder may be felt to be hard and nodular, the spleen is rarely enlarged, and the general cachectic condition of the patient becomes more rapidly exaggerated.

It may be impossible to diagnose between the two conditions, and both may be present at the same time in a patient.

### **Infection of the Bile and its Consequences. Cholangitis, Cholecystitis, and Hepatitis.**

One of the most important dangers of biliary obstruction and stagnation is the great risk which the bile runs of becoming infected by micro-organisms, many of which set up inflammation of the walls of the ducts. Naunyn\* has devoted his attention to this branch of the disease lately, and I quote some of the conclusions which he has come to on the subject.

**Cholangitis.**—Infection of the bile frequently results in a general inflammation of the lining membrane of

\* Op. cit., p. 103, et seq.

the bile-ducts—cholangitis or angiocholitis,—and of the gall-bladder—cholecystitis. The *Bacterium coli commune* is very often the cause of this infection, but staphylococci and streptococci are not uncommonly present when the inflammation takes on a more purulent character. The former bacillus sets up an exudative inflammation of the ducts, and also, at times, a hepatitis. This simple cholangitis, as a rule, only becomes of clinical importance when its frequent sequelæ, cholecystitis and hepatitis or abscess-formation in the liver substance, come on, but it may result in a general and fatal infection of the body, endocarditis being at times set up.

Netter and Martha\* record observations on a case in which there was purulent cholangitis (without any noteworthy hepatitis) and endocarditis, and the bacillus found in the vegetations of the latter was identical with one which was found in the bile. In another case there was no pus in the biliary passages at all, and death resulted from ulcerative endocarditis.

Jaccoud† and Aubert‡ also found the latter condition present in cases of cholangitis. Purulent cholangitis is not infrequent in cholelithiasis, especially when calculi occur in the intra-hepatic ducts. It is occasionally met with when calculi are impacted in the large extra-hepatic ducts, pus lying amongst the stones or between them and the wall of the duct.

\* 'Arch. de Physiol.,' 1886, vol. ix.

† 'Clin. Méd. de Lariboisière.'

‡ "De l'endocardite ulcéreuse végétante dans les infections biliaires," .  
'Thèse de Paris,' 1891.

Occasionally all the ducts behind an obstruction in the common duct are filled with pus.

### **Cholecystitis and Empyema of the Gall-bladder.**

An infectious inflammation is a more serious condition than a simple cholangitis, for very frequently infectious cholecystitis develops, which leads to an empyema, especially when the secretion of the mucous membrane of the bladder cannot escape, but collects and distends the organ.

The contents of a gall-bladder distended as a result of cholecystitis consist of bile, which is rapidly absorbed after closure of the cystic duct, the pathological secretion of the mucous membrane, and pus cells in greater or less profusion according to the severity of the inflammation. In severe cases as much as a litre of pure pus may be found in the distended bladder. Micro-organisms are also generally present.

In most cases the exudative cholecystitis which gives rise to empyema of the gall-bladder is the result of cholelithiasis, and generally the obstructing stone is in the cystic duct or the neck of the gall-bladder, rarely in the common duct. Courvoisier\* traced an association between the cholecystitis and cholelithiasis in 41 out of 55 cases of empyema of the gall-bladder. In Naunyn's experience dilatation of the gall-bladder, when it reaches an extreme degree in ordinary cases of biliary colic, depends not only on simple distension of this organ by the biliary stagnation, but also on an infectious exudative chole-

\* Ref. Naunyn, op. cit., p. 105.

cystitis. He met with five cases of this nature which he records in full.

The inflammation of the gall-bladder may in such cases extend to the peritoneum and cause death from peritonitis, or the infection may become general and cause death with symptoms of septic poisoning. Calculous cholecystitis is not always, however, ushered in by an attack of biliary colic. What is necessary for its development is biliary stagnation, and the entrance of the *Bacterium coli commune*.

In all Naunyn's cases mentioned above, the cholecystitis was ushered in by an attack of biliary colic caused by a stone entering the cystic duct.

In four of the five cases jaundice was absent, and was only slightly marked in the fifth. The liver was but slightly enlarged; fever was absent or only very trifling, with an occasional mild rigor; the distended gall-bladder reached to the umbilicus, and was painful at first, but not so after a few days. The spleen was enlarged to percussion in four cases, and could just be palpated in the fifth. The *Bacterium coli commune* was present in three of the cases. All the patients did well, though the stone probably remained impacted in the cystic duct in every case. The gall-bladder tumour vanished very slowly, the contents being gradually absorbed.

Naunyn is of the opinion that the slight forms of distension of the gall-bladder which commonly result from biliary obstruction are also due to an acute infectious cholecystitis.

Cases of acute infectious cholecystitis which do well for a time are very liable to relapse or to run a

more chronic course. In the latter instance the symptoms are those of a distinct inflammatory affection, or an indolent tumour of the gall-bladder alone remains as the chief abnormal condition.

In chronic cases pyrexia is apt to come on irregularly, but it may be absent altogether. With the exacerbations of temperature the distension of the gall-bladder increases, and it becomes painful once more. Rupture of the distended organ is liable to take place, and adhesions between the gall-bladder and neighbouring organs frequently occur, which generally result in the formation of fistulous communications between the adherent organs.

*Suppuration resulting from the Irritation of the Gall-bladder by retained Calculi.*—A certain quantity of pus or purulent fluid is not at all uncommonly met with, either *post-mortem* or in operations during life, in a gall-bladder which contains calculi without there being any distension of the organ, or what might be called a true empyema of the gall-bladder. Such a condition probably arises from continued irritation of the mucous membrane by the hard foreign bodies which are constantly pressing on it, even though such pressure may be but slight. An infectious cholecystitis is not necessary for the development of this form of suppuration, although of course there must be some degree of local inflammation of the mucous membrane of the gall-bladder resulting from the pressure of the gall-stones, and the pus so formed may contain micro-organisms.

*The Symptoms of Empyema of the Gall-bladder* vary greatly in different cases. In acute empyema, the

patient, with or without previous symptoms of malaise, is suddenly seized with severe abdominal pain, which is most marked in the right hypochondriac region. Symptoms of peritonitis then develop, and fever is generally present. Such cases may terminate fatally in a very few days. Chronic empyema generally begins with an attack of biliary colic, or after symptoms of gastric troubles. Dull pain over the region of the gall-bladder continues, and may be accompanied by pyrexia, and a tumour develops from distension of this organ. The symptoms are, as a rule, very indefinite; colic and jaundice may, or may not, be present.

In some cases it is probable that hydrops of the gall-bladder becomes purulent from the entrance of micro-organisms.

The diagnosis of the nature of the tumour and of the organ from which it arises is arrived at by the methods of physical examination described under "Distension of the gall-bladder."

*Exploratory Puncture of a Distended Gall-bladder*, when undertaken must be made with care, using a fine, short needle and avoiding the edge of the liver and the bowels. Even when the needle can be passed into the gall-bladder without running either of the above risks, the patient is subjected to a source of danger from the great readiness with which the contents of the distended gall-bladder exude even through the finest punctures. Peritonitis ending fatally, as happened in a case recorded by Williams,\* may follow exploratory puncture of a distended

\* 'Brit. Med. Journ.,' Jan. 25th, 1896.

gall-bladder. If exploratory puncture be strongly indicated, precautionary measures to prevent the onset of peritonitis, namely the local application of ice to the abdomen over the swelling, and keeping the patient absolutely at rest, must be taken.

If pus be obtained as a result of the puncture, the diagnosis of the case is made sure.

### Calculous Hepatitis.

Suppuration with the formation of abscesses may be set up in the liver as a result of cholelithiasis. Schröder\* met with this condition nine times in 144 *post-mortems* on cases of gall-stones, but it is very rarely diagnosed during life. Calculous hepatitis may arise in three ways :

1. *An Empyema of the Gall-bladder may Rupture into the Liver Substance* after the formation of adhesions between the inflamed bladder and the lower surface of the liver. Such an event is, however, rare, and only a few cases of this nature have been met with.

2. *The Intra-hepatic Cholangitis at times becomes Purulent*, and invades the liver substance by direct extension, causing the formation of abscesses which may assume different types.

- (a) *Miliary Abscesses* of the size of a millet or hemp seed, and pale in colour, formed by the collection of pus in the fine branches of the inflamed bile-ducts, or by the extension of the inflammation into the hepatic parenchyma (pericholangitic abscesses). This

\* Ref. Naunyn, op. cit., p. 122.

latter condition may be the starting-point of larger hepatic abscesses.

(b) *Inflammatory Destruction of the Wall of the Duct* sometimes leads to the formation of larger biliary abscesses of the size of peas or nuts. They contain a yellowish muco-purulent fluid, pigment, detritus, and small concretions. Their walls may be formed by embryonic and by pyogenic tissue. When there is biliary stagnation the contents of the abscesses have a more greenish tint.

These biliary abscesses may remain discrete and scattered throughout the liver substance, or else many of them come together and form a large focus of suppuration. Two or more such abscesses of the size of apples, connected together by dilated biliary ducts, are at times met with in the liver, the centres of the dilated ducts and the abscesses being filled with a more or less bile-stained purulent fluid, which may contain biliary concretions.

An interesting case, belonging probably to this class of hepatic suppuration, was admitted into the Manchester Royal Infirmary, under the care of Dr. Steell. The case was published by Dr. Steell,\* but I will give a short account of it here.

The patient, a man æt. 34, had for the three years previous to his coming under observation been subject to attacks of pain in the right hypochondriac region, unaccompanied by sickness, and during the latter half of this time he had been jaundiced and had passed clay-coloured stools. Both these symptoms varied in their intensity.

On March 11th, 1892, whilst asleep with his head resting on a table, patient was "struck" with a severe pain in the upper part of the right

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\* 'Manch. Med. Chron.,' May, 1892.

side of the abdomen. He had no rigor. Dyspnœa and cough came on next day, and the pain persisted.

On March 12th, patient was admitted into the Infirmary complaining of severe pain in the right hypochondrium, and of dyspnœa. He was then jaundiced, and appeared to be very ill. Next day as complete an examination as was possible in the patient's serious condition was made, when the liver was found to be much enlarged, and patient complained of pain over this organ. Just below the right costal arch was seen a distinct, localised, obscurely-fluctuating fulness or swelling, which was exquisitely tender. Sitting up in bed increased the pain. Dulness and moist sounds were found over the bases of both lungs.

The temperature on the evening of the 15th was  $103.2^{\circ}$ ; on the morning of the 16th  $101.4^{\circ}$ . Pulse 108, respiration 50.

The local fulness below the right costal arch was punctured with an exploring needle, and a syringe of thick pus obtained. Patient was too ill to bear an operation, so the abscess-cavity was aspirated, and about 1 oz. of thick pus withdrawn. Patient died the same night (March 16th).

*Post-mortem Observations.*—Liver enlarged, weighing 6 lb. 6 oz. The left lobe was specially affected. Surface covered with recent lymph. No gall-bladder could be seen, but the duodenum and neighbouring structures were adherent to the under surface of the liver over its usual situation.

Towards the anterior margin, and extending backwards on each side of the falciform ligament to beyond the middle of the upper surface of the liver, was a large irregular prominence of soft, necrotic tissue. On section, this soft prominence was found to consist of an irregular, acute, infiltrating, suppurative hepatitis. Many bile-ducts distended with yellow bile, and containing blackish biliary concretions, which were soft and gritty, and consisted of bile pigment compounds and cholesterin, were seen.

The gall-bladder was represented by only a small mass of fibrous tissue, which was adherent to the duodenum and neighbouring structures. The cystic duct contained several black calculi, and others were found in the distended hepatic and common bile-ducts. The ostium duodenale was blocked by a club-shaped calculus.

Hæmorrhagic infarcts were found in the lower lobe of the right lung and in the right kidney. The spleen was enlarged. There was no endocarditis.

(3) *Necrosis of the Liver Cells* may result from biliary stagnation, and excite the formation of intra-hepatic abscesses, the necrosed cells being cast off from the surrounding healthy tissue by a process of suppuration. This process has been seen to take place as a result of experimental ligature of the common bile-duct in animals. It was termed "hepatitis sequestrans" by Teuffel.\*

(4) *True Metastatic Abscesses* may form in the liver, the emboli which excite their development being derived from an inflamed gall-bladder, whence they are carried to the portal vein into which the venous blood of the gall-bladder normally passes. From the large branches of the portal vein the emboli enter the liver, and excite suppuration in the small intra-hepatic venules.

The development of these metastatic intra-hepatic abscesses in cholelithiasis may be compared with that which results from suppuration in other portions of the alimentary tract from which the portal vein arises.

*Symptoms of the Hepatic Suppuration*, which develop as a result of cholangitis, are obscure. The most important is the pyrexia, which is generally present. Charcot† described it under the name of "intermittent hepatic fever," and Chauffard‡ thinks that its nature would be more distinctly explained by terming it "intermittent biliary-septic fever." In character it often greatly resembles malarial fever

\* 'Schmidt's Jahrbucher,' 1878.

† Op. cit.

‡ 'Traité de Médecine,' par MM. Charcot, Bouchard et Brissaud, vol. iii, p. 709.

with typical rigors, which, however, in the biliary fever come on generally in the evening, and with irregular intervals of health. Quinine has no effect on the latter fever, nor are the malarial parasites found in the blood. The exacerbations of temperature are often accompanied by attacks of biliary colic, or may alternate with them; they trouble the patient for weeks or months, until death occurs or the calculus escapes from the biliary passages. During the attacks of fever the amount of urea excreted in the urine is greatly diminished, probably because the liver is unable to form any during the pyrexia (Charcot).

Instead of being intermittent, the pyrexia may be more of a remittent type, rising in the evening, falling in the morning, and running a chronic course. Both varieties of fever are to be distinguished from that which accompanies an ordinary attack of biliary colic (q. v.), which is quite of a transitory nature, rarely lasting more than two or three days at the most.

The severity of the pyrexia is not always a true indication of the extent of the suppurative process in the liver, for the temperature may remain normal whilst there is a distinct amount of pus present in the liver.

The pathological cause of the increased temperature is, in all probability, the absorption from the bile into the blood of a toxic body, formed by the micro-organisms present in the former fluid. Enlargement of the spleen is often present in cases of biliary infection.

The development of a cholecystitis with a recog-

nisable enlargement of the gall-bladder, will aid in the diagnosis of angiocholitis, but very frequently the disease is not suspected during life, and is only discovered at the *post-mortem* examination.

### Affections of the Portal Vein.

Affections of the portal vein are occasionally met with in cholelithiasis when the calculi are in the common duct, and also when in the cystic duct and gall-bladder.

Pressure on the main branches of the vein in the hilus of the liver may cause a pylephlebitis which leads to obstruction of the branches of the portal vein in the liver by the formation of a fibrinous clot, or else the pylephlebitis may be of a suppurative type and set up the formation of abscesses in the liver substance.

Occasionally a gall-stone perforates the wall of the common duct, excites the formation of an abscess immediately in contact with the trunk of the portal vein under the lower surface of the liver,\* and this in its turn sets up a pylephlebitis or ruptures into the vein, with the result that metastatic or embolic abscesses are formed throughout the liver.

The diagnosis of affections of the portal vein in cholelithiasis is rarely made during life, although the symptoms which such conditions excite are very severe, as in the following case, which Budd† mentions, in which suppurative pylephlebitis was found *post mortem* in a case of gall-stones.

\* Bristowe, 'Trans. Path. Soc. Lond.,' vol. ix, p. 285.

† Op. cit., p. 176.

A woman, 30 years of age, suffered from a severe attack of illness accompanied by much epigastric pain and jaundice, which was supposed to be caused by the passage of gall-stones. She never completely recovered from the illness, and during the last seventeen months of her life was troubled with "aguish attacks which recurred at irregular intervals varying from a few days to a week. These attacks were generally attended with pain about the liver and jaundice. The spleen was large, and the right lobe of the liver extended down to the crest of the ilium."

Quinine did not improve the case. An attack of severe biliary colic, followed by the passage of a laminated gall-stone in the stools, took place two or three months before death. After the passage of this stone the "aguish" attacks increased greatly in severity, and finally the patient died.

*Post-mortem*, suppurative pylephlebitis was found in the hepatic branches of the portal vein, the main branches in the fissure of the liver containing firm, recent thrombi. An irregular abscess surrounded by gangrenous liver substance, and connected with the suppurating portal vein, was found in one part of the liver. The gall-bladder contained mucus, and its coats were healthy, but marked by the cicatrix of an old ulcer near the neck. The cystic and common ducts were distended, and about an inch from the duodenum a gall-stone, the size of an acorn, was firmly impacted. There was no trace of recent ulceration. The liver and spleen were much enlarged.

## CHAPTER IX.

Ulceration of the Mucous Membrane of the Biliary Passages and its Results—Hæmorrhage into the Biliary Passages—Perforation or Rupture of the Thin Wall of the Distended Bile-duct or Gall-bladder—Local or General Peritonitis.

**Ulceration of the Wall of the Biliary Passages.**

THE constant pressure which is exerted on the wall of the biliary passages by a calculus lodged in one of the larger ducts or in the gall-bladder leads to ulceration of the mucous membrane lining the interior of these structures. The extent of the ulcerative process varies according to the amount of pressure to which the tissues are subjected, and to the length of time during which such pressure persists. In the slighter cases the erosion of tissue is quite superficial, whilst in the more serious ones the ulceration may extend through the mucous and submucous coats to the peritoneal surface of the bile-duct and gall-bladder.

Ulceration of the wall of the biliary passages is a somewhat common, and a very important, complication of cholelithiasis. The importance of this condition is due to the consequences which not infrequently supervene upon the ulceration, and not so much to the ulceration itself.

*Results of Biliary Ulceration.*—In the simpler forms the ulcers will heal rapidly if the irritating

body escapes or is removed, but such cases are rarely met with clinically. It is the more serious conditions which result in symptoms severe enough to attract attention during life.

Ulceration of the walls of the bile-ducts or gall-bladder may result in one of the following conditions :

(1) Hæmorrhage into the biliary passages or liver substance.

(2) Perforation or rupture of the wall of the bile-duct or gall-bladder.

(3) Extension of the inflammation to the peritoneum, with the further development of a local or even of a general peritonitis.

(4) The formation of adhesions between the inflamed peritoneal coats of the ulcerated biliary passage and of the neighbouring organs, which may be followed by ulcerative perforation of the adherent structures, and the formation of a false communication between the adherent organs.

(5) The contraction of the lumen of the biliary passage by the cicatrisation of the ulcer.

(6) The formation of new growths round the ulcer.

**Hæmorrhage into the Biliary Passages** or into the liver substance itself is a very rare complication of cholelithiasis. Still, a few such cases have been recorded. The bleeding takes place as a result of erosion of the small blood-vessels in the wall of the duct, or of the perforation of larger ones in the fissure of the liver either by ulceration or by puncture with a sharp corner of a gall-stone.

Cahn\* had a patient who died after suffering for some time from symptoms—including hæmatemesis and melæna—which might have been caused by a gastric ulcer or by gall-stones. *Post mortem* it was found that a sharp corner of a gall-stone in the cystic duct had set up a “spurious aneurysm” of the right hepatic artery which ruptured into the hepatic duct.

Pauly† has recorded a curious and interesting case in which the patient, a married woman aged 47, with five children, died suddenly in great pain during an attack of cholelithiasis. The *post-mortem* examination showed that the liver substance was very soft, and in it was an extensive fissure from which profuse hæmorrhage had occurred. The extravasated blood had stripped the capsule off a great portion of the right lobe of the liver, and then burst through it into the peritoneal cavity. Many calculi were found in the gall-bladder and bile-ducts. There was no sign of peritonitis. The actual exciting cause of the rupture of the liver substance could not be made out. Pauly suggested that the organ had been softened by the action of micro-organisms.

There were no symptoms during the patient's life to suggest the occurrence of hæmorrhage in this case.

**Perforation or Rupture of the thin Wall of the distended Bile-duct or Gall-bladder,** from the sudden application of pressure external to the biliary system, not infrequently takes place. Cases have been met with

\* ‘Berlin klin. Woch.,’ 1886, p. 353.

† ‘Lyon Médicale,’ 1892, p. 430.

and recorded\* in which this sudden pressure was induced by coughing, vomiting, parturition, and by blows upon the surface of the body over the region of the gall-bladder and liver. Attempts to overcome the obstruction due to an impacted gall-stone by massage over a distended gall-bladder are very likely to cause rupture of the wall of the biliary passages. The rupture may take place whilst the walls of the biliary passages are simply thinned by the distension, or else through the base of an ulcer formed by the pressure of the obstructing gall-stone. If there be no adhesions between the wall of the biliary passages and the neighbouring organs, the contents of the former, when rupture takes place, will escape into the peritoneal cavity. Such an event may terminate fatally through the onset of general peritonitis, especially if the extravasated contents of the biliary passages are purulent or contain infectious micro-organisms.

The escape of non-infectious bile into the peritoneal cavity is not such a serious accident as when the extravasated fluid is infectious. Peritonitis does not readily ensue, and large quantities of bile may be absorbed from the peritoneal cavity. Several cases have also been recorded in which many pints of bile have been removed by "paracentesis abdominis," or by incision and drainage from the abdominal cavity, with subsequent recovery.

In the more serious event of infectious bile entering the general peritoneal cavity, the prognosis is good if the case be diagnosed and laparotomy be done early.

\* Mossé, 'Des accidents d. l. lith. bil.,' Thèse d'agrégation, Paris, 1880.

Mayo Robson\* operated on such a case, in which several pints of bile and pus, which had escaped through a ruptured bile-duct, were removed from a patient who had developed acute peritonitis after suffering from symptoms of gall-stones for twenty-nine years. The patient recovered completely, and was at work in two months from the time of the operation.

A favourable result unfortunately does not always follow an operation in these cases, as the point of rupture may be hard to find, even when in the gall-bladder, and when sought for carefully.

Hawkins† records a case in which a man was suddenly seized with pain in the upper part of the abdomen and with vomiting. As the symptoms continued, and even increased in severity, the abdomen was opened at the end of three days, when acute general peritonitis was found, and two pints of bile-stained fluid were removed from the abdominal cavity. No perforation could be found in the gall-bladder or ducts, although carefully sought for with the fingers, nor could any bile be seen to exude onto the peritoneal surface of these structures on applying pressure to the gall-bladder. The patient died thirty-six hours after the operation, and *post-mortem* an ulcer, one third of an inch in its greatest diameter, was found inside the gall-bladder to the right of the fundus. From the floor of the ulcer a small oblique passage ran to the peritoneal surface of the gall-bladder, opening by a minute orifice through which bile could escape.

As an instance of a successful operation on a ruptured gall-bladder with suture of the perforated ulcer, the case referred to on page 53, in which the rupture came on in the course of an attack of typhoid fever, may be mentioned.

\* 'Brit. Med. Journ.,' April 28th, 1894, Case 73.

† 'Trans. Path. Soc. Lond.,' xliv, p. 78.

*The Symptoms of Rupture of the Biliary Passages* with escape of their contents into the peritoneal cavity, are not unlike those of a ruptured gastric ulcer. Sudden pain over the seat of rupture, followed by more or less pain over the lower part of the abdomen, and the development of symptoms of peritonitis of varying severity according to the nature of the bile which has escaped, and to whether there be any gall-stones or pus-cells in it, are the chief clinical features of such cases.

Jaundice develops in the majority of these cases from absorption of biliary pigment from the peritoneal cavity, and, with the escape of all the bile through the opening in the wall of the biliary passage, the fæces are clay-coloured. When much bile escapes, the diagnostic signs of free fluid in the peritoneal cavity can be made out. Puncture with an exploratory needle may be a useful means of diagnosis in these cases. In addition to the fluid contents of the biliary passages, any gall-stones contained in them may escape into the peritoneal cavity, though this event does not always take place. Instances are frequently met with in literature in which, even after extensive rupture of the gall-bladder wall, none of the concretions have passed into the peritoneal cavity with the escaping fluid. A few cases have, however, been recorded in which gall-stones have been found in the general peritoneal cavity after rupture of the wall of the biliary passages.

Freeman\* found eleven large biliary calculi, resembling chestnuts in size and shape, in the peritoneal

\* 'Bost. Med. and Surg. Journ.,' 1858, p. 337.

cavity and gall-bladder of a patient who had died after severe symptoms of general peritonitis. Three pints of bile-stained sanguineous fluid were also present in the abdominal cavity. There was an opening one and a half inches in diameter midway between the fundus of the gall-bladder and the common duct, through which the contents of the gall-bladder had escaped. Thorowgood\* records a similar case.

Cases are more frequently recorded in which gall-stones have escaped from the gall-bladder through an opening in its wall and have become encysted by local peritoneal adhesions close to the point of rupture, without the general peritoneal cavity being at all affected. The adhesions have in such cases probably formed before the perforation takes place. Sharman† met with such an instance in the dissecting-room, the rupture of the gall-bladder having evidently taken place some time previously, and having been cured spontaneously. Simon‡ recorded two cases in which the cyst containing the concretion communicated with the gall-bladder. A local abscess is often formed by the escape of the fluid and calculi from the biliary passages in these cases. These abscesses are generally situated under the liver, in contact with the duodenum or colon, but occasionally one is formed under the diaphragm after the rupture of the gall-bladder. Morton§ made a *post-mortem* examination of a case in which a primary perforation of the gall-

\* 'Lancet,' 1868, vol. ii, p. 764.

† 'Med. Times and Gaz.,' 1859, vol. i.

‡ 'Path. Trans.,' vol. v.

§ 'Lancet,' March, 1893, vol. i, p. 586.

bladder was followed by the formation of a localised cavity by the colon, omentum, and liver, which acted as a secondary gall-bladder, and contained some gall-stones. Later on, however, this secondary gall-bladder cavity ruptured into the general peritoneal cavity, and caused death.

It is almost impossible to diagnose such local abscesses unless they point superficially towards the wall of the abdomen, and as they tend to work their own cure by bursting into a neighbouring organ—generally the intestinal tract—or superficially through the abdominal wall, they are not often met with surgically. They will be referred to later on under the description of the formation of fistulous passages.

### Local or General Peritonitis.

The inflammation round an ulcer in the wall of the biliary passages not uncommonly extends to the neighbouring peritoneum, and excites local or even a general peritonitis. The former condition is a common occurrence in cholelithiasis, and results in the formation of adhesions between the biliary passages and the neighbouring structures.

The importance of this local peritonitis is not on account of the adhesions which result from it, but because of the consequences of such adhesions, namely, the formation of false passages between the gall-bladder or bile-ducts and the organs or tissues to which these structures adhere. This condition will be referred to more fully in the next chapter, in

the paragraphs on biliary fistulæ. A local peritonitis around a gall-bladder may involve the colon, and cause intestinal obstruction by paralysing the walls of the bowel. A case of this nature is mentioned in the chapter on intestinal obstruction from gall-stones (p. 216). A case of general peritonitis, probably arising from extension of inflammation from the gall-bladder to the abdominal peritoneum, was referred to by Lauder Brunton at a meeting of the Medical Society of London, in January, 1896.\*

The patient, a married woman æt. 32, had complained of pain in the right iliac region for two or three years. Nothing was discovered on examination. The urine contained oxalate of lime, etc. The pain came on in paroxysms, and passed towards the umbilicus. It was supposed to be renal; there had never been any jaundice. She left England for five years, during which time she had several severe attacks of pain in the right side with symptoms of peritonitis. In June, 1893, she was examined again, and a lump, first noticed two years previously, was found below the liver, which had been diagnosed to be an enlarged gall-bladder or possibly a floating kidney. While the patient was on her back the tumour could be pressed up under the ribs, and it seemed to be dragged upon during respiration. In September, 1894, she gave birth to a child, and in December she was seized with vomiting and died of peritonitis. The tumour became very tender during the attacks. In addition to its mobility and its connection with the liver, there was a history of pain passing towards the umbilicus. *Post mortem* the gall-bladder was found to be greatly enlarged, and to contain many gall-stones, the largest of which measured an inch in diameter.

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\* 'Brit. Med. Journ.,' Feb. 1st, 1896, Case 8.

## CHAPTER X.

Inflammatory Adhesion of the Biliary Passages to the Neighbouring Organs and Tissues—Varieties of Biliary Fistula—Fistulous Communications between the Biliary Passages and the Alimentary Tract—Varieties: Hepato-gastric, Biliary-gastric, Biliary-duodenal, Biliary-intestinal, and Biliary-colic—Symptoms indicative of the formation of Biliary-intestinal Fistulæ—Biliary-urinary, Biliary-vaginal, Biliary-thoracic, Biliary-cutaneous, Biliary-retro-peritoneal, and Biliary-portal Fistulæ.

**Inflammatory Adhesion of the Biliary Passages to the Neighbouring Organs and Tissues.**

WHEN the ulceration in the wall of the biliary passages extends to the peritoneum, a peritonitis is set up, which, in the majority of cases, remains local, extending only to the organs and structures immediately adjoining the original seat of inflammation. This is most often found to be in the gall-bladder; and as the duodenum, colon, small intestines, and abdominal wall are in immediate relation to this organ, the peritoneum covering them is excited to inflammation, and, as a rule, by direct contact with the primary inflammatory focus. As a result of the inflammation of two portions of peritoneum lying in apposition to each other, adhesions generally form, which unite the organs beneath the inflamed tissues to each other. The process may stop at this point, and, the acute condition subsiding, the adhesions

remain permanent, but excite no symptoms and cause no inconvenience.

*Biliary Fistulæ.*—But, instead of this termination, the ulcerative inflammatory process may go on and cause the erosion of tissue which results in the formation of a “false” or “fistulous” passage between the biliary passage and the organ to which it is adherent.

Instead of the inflammation extending from the primary focus by direct contact, it may arise through the medium of a local abscess which forms in the peritoneal cavity around the primary focus of inflammation in the biliary passage, and which excites inflammation and erosion of the tissues and organs surrounding it. The most important result of the above direct or indirect extension of inflammation to the neighbouring organs is the formation of false passages between them and the biliary system.

The formation, then, by gall-stones, of fistulous communications between the biliary system and the neighbouring organs or the external surface of the body takes place, either by direct adhesion of the inflamed wall of the bile-duct or gall-bladder to the neighbouring structure involved in the process, with consequent ulceration of the tissues intervening between the irritating calculus and the new position to which it is endeavouring to make its way, or indirectly through the medium of a localised abscess outside the biliary passage (pericholitic), which ends in the formation of the abnormal passage by rupturing or eroding through the structures opposing the further progress of the calculus.

### Varieties of Biliary Fistula.

There are several varieties of biliary fistula, some more common than others, and cases have been, and still are, frequently recorded, in which one or other form develops in cholelithiasis. Courvoisier and Naunyn\* examined the published cases, and the following table shows the various forms of biliary fistula and the number of cases of each variety which they found recorded in medical literature.

Between the biliary passages themselves	.	.	8
„ „ „ and the stomach	.	.	12
„ stomach and the liver	.	.	4
„ „ „ gall-bladder	.	.	8
„ biliary passages and the duodenum	.	.	108
„ duodenum and the common bile-duct	15		
„ „ „ gall-bladder	.	93	
„ jejunum „ „	.	.	1
„ ileum „ „	.	.	1
„ biliary passages and the colon	.	.	50
„ colon and the gall-bladder	.	49	
„ „ „ common bile-duct	.	1	
„ biliary passages and the urinary passages	.	.	6
„ „ „ „ thoracic organs	.	.	10
„ „ „ „ abdominal walls	.	.	184
„ „ „ „ retro-peritoneal tissues	.	.	4
			<hr/> 384

It must be pointed out, however, that these figures are not a true estimate of the relative frequency of the various forms of fistula, the gastro-intestinal communications being often overlooked or not recorded, whilst probably all those in connection with the urinary and thoracic organs are published on

\* Op. cit., p. 134.

account of their rarity. Biliary-cutaneous fistulæ always attract attention, and seem to be recorded in larger numbers than their relative frequency warrants.

The following figures, taken also from Naunyn, give a more correct view of the relative frequency of the various forms of biliary fistula. Out of a total of 10,866 *post-mortem* examinations made by Roth, Schröder, and Schloth on all affections, evidences of cholelithiasis were found 1029 times. Biliary fistulæ occurred in 43 of these 1029 cases, in two others the gall-bladder was perforated, and in one other case the cystic duct was ruptured, the contents of the biliary passages escaping into the peritoneal cavity in the three last cases.

The forty-three cases of fistula occurred as follows :

Between the biliary passages themselves	.	.	1
„ the gall-bladder and the liver	.	.	1
„ „ „ stomach	.	.	1
„ „ „ duodenum	.	.	19
„ „ „ colon	.	.	16
„ the common bile-duct and the duodenum	.	.	5
			<hr/>
			43

### Fistulous Communications between the Biliary Passages and the Alimentary Tract.

**Hepato-gastric Fistulæ.**—Fistulous communications between the liver and the stomach are rare. When they do occur they are generally formed by the adhesion of the left lobe of the liver to the stomach, with consequent rupture of a dilated bile-duct into the cavity of the latter organ.

**Biliary-gastric Fistulæ.**—The gall-bladder occa-

sionally adheres to the stomach close to the pyloric orifice, and perforation ensues through which the irritating concretion escapes from the biliary passages. Although liquids do undoubtedly pass, at times, from the duodenum back through the pylorus into the stomach, Murchison and others are of the opinion that all gall-stones—at any rate the larger ones—which are vomited must enter the stomach through a fistulous communication with the bile-ducts or gall-bladder, as it would be very difficult for a solid body the size of a nutmeg to pass backwards through the pylorus. In one case Jeaffreson\* found *post-mortem* such a false passage through which a gall-stone, which had been vomited some time previously, had passed. Other observers have recorded similar cases.

A good instance of the vomiting of gall-stones is recorded by Miles.†

The patient, a woman æt. 56, had suffered from symptoms of gall-stones for two or three years, when she began to be troubled with persistent daily vomiting of about three to four pints of brownish fluid which contained *Sarcinæ ventriculi*. This condition continued for a couple of years, when she was seized with intense pain over the stomach and right side, which was followed by violent sickness, during which she vomited a large flattened gall-stone  $\frac{7}{10}$  by  $\frac{5}{10}$  of an inch in size. After this her symptoms became much easier and she improved for two weeks, when, after a similar attack, she vomited another gall-stone of equal size to the first. Her condition then improved steadily, the vomiting ceased, and she eventually made a good recovery.

*Pyloric obstruction* occasionally occurs in cholelithiasis, and is brought about when a large gall-stone in the fundus of the gall-bladder or in the common

\* 'Brit. Med. Journ.,' May 30th, 1868.

† 'Lancet,' 1861, vol. i, p. 57.

bile-duct, which is endeavouring to form a false passage into the stomach, presses on the pylorus and obstructs the outflow of the contents of the stomach through it. As a result of this obstruction, symptoms of gastric dilatation come on. When the stone escapes into the alimentary tract the obstruction may be relieved, and the secondary gastric symptoms disappear, as happened in Miles's case referred to above.

But occasionally the irritation due to the formation of the fistula sets up inflammatory changes in the wall of the pylorus, leading to increase of the fibrous tissue there, and permanent stenosis of the orifice.

Hale White\* made a *post-mortem* on a case in which this condition was present, and in the thickened tissue was a small pea-sized cavity containing a few small faceted gall-stones, which opened into the duodenum by a short sinus. The gall-bladder was adherent to the pylorus opposite the cavity, but did not communicate with the latter, although it seemed from the appearances present in the gall-bladder that a passage had formerly existed. Several calculi were found in the gall-bladder. The patient died from the results of the pyloric stenosis.

Other cases of stenosis of the pylorus have been recorded.

It is possible that a perforation of the stomach, caused by the passage of a gall-stone, might, in cicatrising, result in a narrowing of the pyloric orifice, but I know of no recorded cases of this nature.

**Biliary-duodenal Fistulæ.**—Fistulæ between the common bile-duct and the duodenum consist chiefly of those formed by the enlargement of the ostium

\* 'Trans. Path. Soc. Lond.,' xxxvii, p. 280.

duodenale of the common bile-duct by erosion of its edges caused by the passage of a concretion which is too large to escape through the orifice by simply dilating it. The importance of this condition has been emphasised by Roth\*, who pointed out that if the supposed extreme, but apparently simple, dilation of the ostium duodenale of the common bile-duct frequently met with in cholelithiasis be carefully examined, evidences of erosion of the edges of the orifice will often be found.

Roth\* met with such a condition five times in 25 cases of biliary fistula (from a total of 535 *post-mortems* on cases of cholelithiasis), whereas Schröder\* and Schloth\* did not observe it once in 21 cases of biliary fistula (from a total of 494 similar *post-mortem* examinations).

It is very probable that more or less erosion of the edges of the ostium duodenale is caused by the passage of all hard calculi bigger than peas. The process concerned is generally of a simple nature, a long-continued pressure from a firm concretion gradually, but surely, causing an ulcerative erosion of the resisting tissues in contact with it; or else it is of a more rapid, tearing nature, when an irregularly-shaped concretion is escaping (Ord†).

**Gall-bladder-duodenal Fistulæ.**—From the above tables it will be seen that this is the commonest form of biliary-intestinal fistula, and that the next in order of frequency is that between the gall-bladder and the colon. This is explained by the anatomical

\* Ref. Naunyn, op. cit., p. 135.

† 'Brit. Med. Journ.,' March 5th, 1887.

relations of the gall-bladder with the neighbouring structures. To quote from Quain's 'Anatomy':—"The gall-bladder rests below on the commencement of the transverse colon, and farther back it is in contact with the duodenum, and sometimes with the pyloric extremity of the stomach."

It is easy, then, to understand how an inflamed gall-bladder may adhere to the duodenum, colon, or occasionally to the stomach. When once the adhesion is made, the process of ulceration in time extends through the coats of the adherent organ, or else the localised abscess outside the gall-bladder bursts through the wall of the intestine or stomach, and the fistulous communication between the two organs is made, the stone escaping from the one into the other.

In some cases the fistulous opening into the duodenum remains too small to allow of the escape of the calculus, but will permit bile to flow freely into the intestine. Chadwick's case, referred to previously, is an instance of such a condition.

The gall-bladder, in the majority of cases, adheres by its fundus to the horizontal portion of the duodenum, and a fistulous opening is rarely found in the neck of the former organ.

In addition to being the commonest form of biliary-intestinal fistula, a gall-bladder-duodenal fistula is probably more often met with than any other biliary fistula, for the large number of false passages through the abdominal walls, which Courvoisier found recorded in literature, conveys an erroneous impression as to the relative frequency of these two forms of biliary fistula.

Gall-bladder-duodenal fistulæ are very important clinically, apart from their frequent occurrence, because the largest calculi escape into the intestine through them, and the patient is thereby subjected to the many dangers which arise during the passage through the whole length of the small intestine, and through the ileo-cæcal valve, of such large foreign bodies. Calculi which enter the duodenum through a common duct fistula, have, of course, as far to travel, but these latter concretions are much smaller as a rule than those which escape directly from the gall-bladder. The largest concretions escape from the gall-bladder through a false passage between it and the duodenum or colon. It is not at all uncommon for calculi the size of pigeons' or even hens' eggs to work their way through such a channel into the lumen of the bowel, whilst those which escape through a common duct fistula are rarely larger than hazel-nuts or walnuts.

*The Small Intestine* is but rarely involved in the formation of biliary fistulæ, and need not receive separate mention here.

**Gall-bladder-colic Fistulæ**, if almost as frequent, are by no means so important clinically as those in connection with the duodenum; for although large biliary concretions escape through them, they have avoided by a short circuit the dangers of the passage of the small intestine and ileo-cæcal valve. When even the largest concretions are once in the cæcum they generally manage to pass out without any trouble; they do, however, at times set up serious or fatal obstruction, as will be mentioned later on.

As a rule the existence of a gall-bladder-colic fistula is only discovered at a *post-mortem* examination, and this form of fistula is sometimes present in the same case with one between the biliary passages and the duodenum. In the majority of cases the gall-bladder adheres to the transverse portion, and occasionally to the hepatic flexure of the colon.

Coe\* mentions a curious case in which a patient had for a long time "suffered from very violent and almost constant pain, the cause of which was found, on opening the body, to have been that a large stone in the gall-bladder had so compressed the colon as to wear the coats of it, while the coats of the bladder itself had no apparent marks of injury."

The dangers which may arise from the presence of biliary calculi in the intestinal tract will be referred to in the next chapter.

### Symptoms Indicative of the Formation of Biliary-intestinal Fistulæ.

The formation of biliary-intestinal fistulæ with the escape of large concretions frequently takes place without exciting any unusual symptoms. The following case recorded by Smith† is of interest in this respect.

On May 30th, 1894, a woman, æt. 63, was admitted to the Manchester Royal Infirmary with symptoms of acute intestinal obstruction of six days' duration. She had had no previous attacks of pain, nor had she suffered from any gastric symptoms even, but she had lost weight in the previous eighteen months. The illness for

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\* Op. cit.

† 'Manch. Med. Chron.,' April, 1895.

which she was taken into the hospital began on May 24th with sudden, severe pain and vomiting, coming on after her dinner. She got worse, and was in a very bad condition on the 30th. The case was considered to be one of obstruction from fæcal impaction, and was operated on. A gall-stone  $1\frac{1}{2}$  inches long,  $3\frac{3}{8}$  inches in circumference, and weighing  $\frac{1}{2}$  ounce, was removed from the middle of the jejunum. The patient died, and *post-mortem* the gall-bladder was found adherent to the duodenum  $1\frac{3}{4}$  inches below the pylorus, and a large fistulous communication between the two organs existed.

Blackburn\* mentions an instance in which a woman, æt. 45, without aggravation of the usual signs of the passage of a gall-stone, passed *per anum* one  $3\frac{3}{8}$  inches long by  $1\frac{1}{2}$  thick, and weighing 1 oz. 6 drachms.

On the other hand, patients frequently suffer from severe but indefinite pain in the region of the gall-bladder, the nature of which is often unsettled until a large gall-stone is passed *per anum*, or symptoms of intestinal obstruction, due to the impaction of a gall-stone in the bowel, come on.

The diagnosis during life of the formation of fistulous communications between the biliary system and the stomach or intestinal tract can only be made in favorable cases. If a case which has suffered for some time from symptoms of biliary obstruction suddenly improve, and a large stone be passed *per anum*, or be vomited, there cannot be much doubt as to the nature of the case. Hæmatemesis, or mælena, associated with pain in the epigastric or right hypochondriac regions, and especially when accompanied by jaundice, must make one suspicious of the formation of a biliary-intestinal fistula; and a large

\* 'Lancet,' Dec. 12th, 1868.

stone can, at times, be felt through the abdominal parietes in the region of the gall-bladder.

Symptoms of pyloric stenosis associated with hæmatemesis, jaundice, and other symptoms of cholelithiasis, will suggest the presence of a gall-stone eroding its way through the coats of the stomach.

*Hæmorrhage* into the stomach, duodenum, intestines, or externally through a superficial opening, is a serious and by no means uncommon result of the ulcerative process which is concerned in the formation of fistulous communications between the biliary passages and the neighbouring organs, or the surface of the body through the abdominal parietes. It is indicated during life by the occurrence of hæmatemesis, or melæna, and the loss of blood may be serious enough to cause death. As a good instance of a fatal result Duffet's\* case may be mentioned :

The patient, a man æt. 52, had suffered from biliary colic for nine years, gall-stones being found in the motions at times. On March 24th, 1895, he vomited more than a pint of dark, partially-clotted blood. He became jaundiced and suffered from itching of the skin, but had no pain. Stools clay-coloured, urine contained bile pigment. On April 8th he over-exerted himself, and again vomited a pint and a half of semi-fluid, dark blood just as he was sitting down to tea. Two hours afterwards he vomited half a pint more blood, and passed some loose motions containing blood. He was much collapsed. Next morning, ten hours after the last attack of vomiting, he brought up three pints of clotted blood and died in about twelve hours.

*Post-mortem.*—A communication between the gall-bladder and duodenum was found, these organs being firmly adherent to each other, and lying loose in the duodenum was an unfaceted gall-stone and a quantity of blood. The edges of the opening were soft and

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\* 'Brit. Med. Journ.,' May, 1895.

probably of recent date. The gall-stone measured  $\frac{3}{4}$  by  $\frac{1}{2}$  an inch in diameter, and weighed when dry 40 grains.

Chadwick's case referred to above also probably died from the results of severe hæmorrhage, but although there was a fistulous communication between the duodenum and the biliary passages, it was of old standing, and the blood escaped from the œsophageal plexus of veins, or from those in the stomach, and was probably more of the nature of a hæmorrhage of hepatic cirrhosis. Chadwick attributed the hæmorrhage to the interstitial changes in the liver, and to the enormous congestion of the spleen.

Ord\* published two interesting cases of hæmorrhage associated with the passage of gall-stones. In the first it preceded the passage of a large stone, which took place without there being complete biliary obstruction. The bleeding was probably caused by tearing of the wall of the duodenal orifice of the common duct. In the second case the hæmorrhage occurred directly after an attack of biliary colic accompanied by jaundice. After cessation of the mælena a ragged gall-stone was found, and a few days later, after a slighter attack of hæmorrhage, a smaller stone appeared in the stools. The bleeding in the latter case probably came from a torn ostium duodenale of the common duct. In both cases it appeared in the stools only.

In cases of hæmatemesis the fistula, from the walls of which the bleeding has taken place, need not be in the stomach, but if it be in the duodenum the blood

\* 'Brit. Med. Journ.,' March 5th, 1887.

very frequently regurgitates back through the pylorus into the stomach, and is then vomited.

### Biliary-urinary Fistulæ.

A fistulous communication between the biliary and urinary systems is a very rare occurrence. Fauconneau-Dufrésne,\* Pelletan,† Güterbock,‡ and Faber§ and Köstlin,|| &c., have referred to such cases.

Güterbock removed a biliary concretion of the size of a walnut, and other smaller ones, by lithotripsy from the urinary bladder of a woman who had previously passed *per urethram* three small faceted gall-stones. Faber's patient, also a woman, passed sixteen biliary calculi, varying from 7 to 40 grains in weight, during a period of close on two years. When this patient died, twenty-five years after Faber's observations on her, Köstlin made a *post-mortem* examination of the body, and found a fibrous band running from the middle of the lower margin of the liver in front of the intestines to the urinary bladder. This band consisted of two parts,—the lower the remains of the urachus, the upper of the gall-bladder. There were no concretions in either the gall or urinary bladders. The distended gall-bladder may unite with the pelvis of the right kidney (Fauconneau-Dufrésne).

In Pelletan's case a tumour developed in the right

\* 'Gaz. Méd. de Paris,' 1840.

† 'Journ. de Chim. Méd.,' 2nd series, vol. ii, Nos. 11 & 12.

‡ 'Virch. Arch.,' vol. lxi.

§ 'Schm. Jahrb.,' 1840.

|| 'Deutsch. Klin.,' 1864, p. 116.

iliac region of a woman, without any previous symptoms of peritonitis. This persisted for some time, and then symptoms of cystitis developed, and in two months' time biliary calculi were voided in the urine. In eight days 200 almost pure cholesterin stones were passed in this way.

The symptoms excited by biliary-urinary fistulæ are mostly suggestive of affections of the latter organs. Cholesterin in the urine does not of necessity indicate the presence of biliary calculi in the urinary passages. Murchison\* only met with it once, and that was in a case of calculous pyelitis, with no communication with the biliary passages, and Roberts† also saw cholesterin in the urine of a patient suffering from hæmaturia with symptoms of a calculus in the left kidney.

#### Biliary-vaginal Fistulæ.

Fistulous communications between the biliary passages and the female genital organs are very rare. Only one distinct case is recorded (by Frank‡ in 1790). The patient complained of severe pain on the right side of the uterus, in which situation a tumour could be felt. After this condition had persisted for some time without much alteration, pus began to escape *per vaginam*, and finally a gall-stone was discovered in the discharge. Twenty-five others were shortly afterwards passed *per rectum*, preceded by severe symptoms, including pain and jaundice. The patient recovered eventually.

\* Op. cit., p. 555.

† 'A Practical Treatise on Urinary and Renal Diseases,' 4th edit., p. 134.

‡ Ref. Courvoisier, op. cit., p. 110.

### Biliary-thoracic Fistulæ.

Biliary-thoracic fistulæ are extremely rare, and only a few cases have been recorded.

The fistulous communication generally arises from an abscess on the upper surface of the liver which is connected below with the bile-ducts, and which establishes a communication, by erosion of a passage through the diaphragm, with the bronchial tubes of the lungs, with the mediastinum, and the pericardial or pleural cavities.

The abscess-cavity on the surface of the liver is generally the result of suppurative cholangitis which is set up by gall-stones in the small intra-hepatic, or in the larger extra-hepatic ducts.

### Biliary-pulmonary Fistulæ.

Fistulous communications between the biliary passages and the lungs are rare. One or two cases have been recorded in which bile, or bile-coloured sputum, was expectorated during life, and *post-mortem* a communication between the biliary passages and the bronchial tubes was found.

One very interesting case is described by Dreschfeld.\*

The patient was admitted to the Manchester Royal Infirmary suffering chiefly from the expectoration of large quantities of bile, which had been going on for seven months at least. He was not jaundiced, and there were no symptoms of biliary colic. The general condition was very bad, and the patient died shortly after admission to the hospital.

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\* 'Lancet,' Dec. 13th, 1879.

*Post-mortem*, the right lung and right lobe of the liver were adherent to the diaphragm. On section through the adherent lung and through the liver, several of the intra-hepatic bile-ducts were found to be dilated and to contain pus. These dilated ducts communicated with a small abscess-cavity near the upper surface of the liver, which also contained, besides thick pus, a small irregular gall-stone. A sinuous passage led from this cavity through the diaphragm to the bronchial passages of the right lung.

The common bile-duct was patent, the cystic duct closed, and the gall-bladder dilated with mucus. No other calculi were found. The liver, except near the dilated bile-ducts, was normal.

Another case of biliary-pulmonary fistula, recorded by Bristowe,\* is similar to the above.

### Biliary-pericardial Fistulæ.

A case of a subdiaphragmatic hepatic abscess communicating with the pericardium occurred in the experience of Legg.† There was found *post-mortem* an abscess on the upper surface of the left lobe of the liver which communicated with the pericardial sac through two perforations in the diaphragm 10 millimetres in diameter. Dilated bile-ducts opened into the abscess from the liver. The common duct was obstructed by a stone as big as a hazel-nut. Bile had been able to pass by the stone, and jaundice only occurred during the last fourteen days of life.

### Biliary-mediastinal Fistulæ.

Simmons‡ has recorded the case of a man, æt. 24, in which an abscess, commencing round the gall-bladder, extended upwards and to the left,

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\* 'Trans. Path. Soc. Lond.,' vol. ix, p. 285.

† Ibid., xxv, p. 133.

‡ 'Am. Journ. Med. Sci.,' 1877.

and burst into the mediastinum, and through that by a very small opening into the right bronchus. Six gall-stones were found in the gall-bladder. The symptoms which appeared during life are interesting. Two years before the final illness he suffered from an abscess in the right hypochondriac region, which burst superficially, discharged some "dark-coloured matter" for some time, and then healed up. When first seen by Simmons in the final illness the man was very ill, and complained of severe pain in the epigastric region. An indistinct, circumscribed swelling was found in this region dipping down towards the right hypochondrium. Indistinct fluctuation was felt over it, with a sense of intervening air or gas, which was verified by percussion. A blowing sound, synchronous with respiration and accompanied occasionally by a gurgling noise, was heard with the stethoscope. The lungs and pleuræ were normal to percussion and auscultation. The heart was pushed across to the left, and its action was laborious. There was no expectoration of pus or bile during life. There was a large amount of pus formed in the mediastinal and hepatic abscess-cavities at the *post-mortem*.

### Biliary-pleural Fistulæ.

As an instance of a biliary fistula opening into the pleural cavity, Cayley's\* case may be referred to. In this the bile-ducts were dilated, and opened into an abscess on the upper surface of the left lobe of the liver, which communicated further with the left pleural cavity by means of a small perforation through the diaphragm. The bile-ducts were all widely dilated. No gall-stone was found, but there was a previous history of burning pain in the epigastrium, and rigors, followed by enlargement of the liver, and jaundice.

### Biliary-cutaneous Fistulæ.

Out of 137 recorded cases in which the information was given, Courvoisier† found that this form of fistula

\* 'Trans. Path. Soc. Lond.,' 1866, p. 160.

† Op. cit., p. 116.

occurred in 17 men and 37 women below the age of fifty, and in 16 men and 67 women over that age, whereas Murchison\* considers that the affection nearly always occurs in females of middle or advanced age.

From the number of cases in Courvoisier's table (p. 191), it would seem that this form of biliary fistula is very common, especially when compared with the other forms recorded there, but this impression is immediately corrected when it is noticed that in not one instance was the fistula met with by three observers in a total of 10,866 *post-mortems* on patients who had died from various diseases, in which gall-stones were found in 1029 different cases. The condition is, in fact, not at all common.

The explanation of the large number found recorded in medical literature by Courvoisier is probably that biliary-cutaneous fistulæ can be recognised during life, and are almost impossible to overlook; and as it is a most interesting condition, a very large proportion of the cases in which it occurs is published in the medical journals. Biliary-intestinal fistulæ, on the other hand, require a *post-mortem* examination for their recognition, permission for which can only be obtained in a small minority of patients who die. The material, therefore, from which statistics of the former affection are drawn up is much greater than that available for cases of biliary-intestinal fistulæ, and it is quite unfair to compare the relative frequency of the two affections by the number of cases recorded in general medical literature. The second

\* Op. cit., p. 556.

table is a much more reliable statement of the prevalence of the various forms of biliary fistula. Biliary-cutaneous fistulæ are formed either by direct adhesion of the gall-bladder to the parietal peritoneum on the anterior abdominal wall, with consequent erosion of the abdominal parietes, or else through the medium of a localised abscess which has formed around that part of the extra-hepatic bile-duct or gall-bladder wherein the irritating calculus is lying, as a result of perforation of the wall and escape of bile, &c., and which works its way through the intervening parietal tissues to the surface. Direct adhesion of the gall-bladder to the anterior abdominal wall is generally set up by empyema of the former organ.

The first evidence of the formation of a biliary-cutaneous fistula is often afforded by the appearance of a subcutaneous abscess in the neighbourhood of the umbilicus, which either bursts or is opened surgically, and bile-stained pus escapes.

When external biliary fistulæ develop through the medium of an abscess around the gall-bladder or common duct, they most frequently appear in the region of the umbilicus, the pus tracking down from the under surface of the liver along the remains of the umbilical vein, in the suspensory or falciform ligament of the liver. But the cutaneous opening may be in the right inguinal region, over the pubes, or even above the clitoris. It is found not infrequently to the left of the median line, and almost anywhere to the right of this line and above or below the umbilicus. The region of the umbilicus is, however,

the commonest situation for the external fistulous opening.

Calculi of various sizes and shapes escape from the biliary passages through cutaneous fistulæ. A case in which a large oval calculus, weighing 170 grains when dry, and measuring 3 inches in its smallest and  $3\frac{5}{8}$  inches in its greatest diameter, escaped through an opening in the right hypochondriac and epigastric regions, occurred in the practice of Gutteridge.\* The patient had been subject to previous attacks of biliary colic, and then an abscess developed in the epigastric and right hypochondriac regions, which burst and discharged pus for about six weeks, when the large concretion escaped through the opening. Fauconneau-Dufrésne† refers to a calculus 3·15 inches in length by 1·1 inch in breadth, which escaped through a biliary-cutaneous fistula.

Instances of the escape of smaller calculi are common. Good examples of such cases are recorded by Yeldham‡ and Cookson.§ In the former the abscess was opened surgically.

Even when there is no obstruction in the common bile-duct, biliary-cutaneous fistulæ generally remain open until all the irritating calculi have been discharged,—an event which may not happen for months or years. In more favorable cases they may close more rapidly, and Murchison|| refers to a case in which the fistula healed up in ten weeks.

\* 'Lancet,' 1878, vol. i, p. 851.

† Ref. Murchison, op. cit., p. 557.

‡ 'Lancet,' 1878, vol. i, p. 113.

§ 'Lancet,' 1878, vol. i, p. 30.

|| Op. cit., p. 558.

If there be an obstruction in the common duct to the flow of bile into the intestines, the fistula remains permanent, and so also as long as the cystic duct is closed. Surgical aid will often hasten the closure of the cutaneous opening of the fistula, especially if all the gall-stones have escapèd from the biliary passages. In more troublesome cases the gall-bladder may be excised, or an artificial gall-bladder-intestinal fistula be made.

*The Nature of the Fluid which escapes* varies according to whether the large bile-ducts are patent or obstructed. If the cystic duct be closed, a clear, viscid mucus, containing at times more or less pus, and occasionally cholesterin, escapes; but if this duct be open, a certain amount of bile is present in the discharge. If the common duct be obstructed whilst the cystic duct is free, all the bile will escape through the fistula. Some patients do not seem to suffer at all from the loss of their bile, but others get into a low cachectic condition in time, especially if much pus be formed and escape through the opening.

Biliary calculi are also discharged through the fistulous opening, and may continue to come away for some months after the onset of the condition. The discharge may also persist after all the calculi have escaped, or it may be some long time after the formation of the fistula before any concretions pass out through it.

When the external opening of the fistula is much below the normal situation of the gall-bladder, the channel through the abdominal wall connecting it

with the latter organ is often long and sinuous, and its walls are indurated and thickened.

### Rarer Forms of Biliary Fistula.

The other forms of biliary fistula mentioned in Courvoisier's table are very rare.

#### *Biliary-retro-peritoneal.*

Naunyn\* had a patient who suffered chiefly from ascites and jaundice, and who died soon after he saw her. *Post-mortem*, a large stone was found at the duodenal end of the common duct, the duct itself being much dilated, and perforated in one place. The perforation led into a cavity behind the peritoneum, which was full of bile-coloured pus and bilirubin-calcium detritus. The abscess extended downwards behind the ascending colon to the right iliac fossa, but not affecting the vermiform appendix, and inwards to the inferior vena cava, the wall of which was perforated. Inside that vein was a clot which contained masses of what was apparently bilirubin-calcium detritus.

*Biliary-portal Fistulæ* are very uncommon. A perforation of the wall of the portal vein in the fissure of the liver when it occurs is generally the result of an abscess, formed round the gall-stone in the duct, breaking through into the lumen of the vein (Bristowe).† Murchison‡ (Case clxxxviii) found a gall-stone in the lumen of the portal vein.

Thrombosis or pylephlebitis and consequent hepatic suppuration are excited by the formation of the fistula.

\* Op. cit., p. 135.

† 'Trans. Path. Soc. Lond.,' vol. ix.

‡ Op. cit., p. 579.

## CHAPTER XI.

Biliary Calculi in the Intestinal Tract—Intestinal Obstruction from Gall-stones, and its Varieties—Intestinal Obstruction from the Impaction of a Gall-stone in the Lumen of the Bowel—Age of the Patients—Length of Time during which a Calculus may remain in the Bowel—Situation of the Obstruction—Duration—Prognosis—Recurrent Attacks—Biliary Calculi in the Vermiform Appendix, and in the Colon and Rectum—Symptoms of Intestinal Obstruction from Gall-stones—Diagnosis of the Seat of the Obstructing Stone—Perforation of the Intestine—Stricture of the Intestine.

**Biliary Calculi in the Intestinal Tract.    Intestinal  
Obstruction from Gall-stones.**

THE majority of calculi which pass out from the biliary system through fistulous communications with the intestinal tract escape from the body without causing any trouble. They may either be vomited or pass out in the stools. Calculi of various sizes leave the body in either way, but in the great majority of cases by the latter channel. Some as large as nutmegs have been vomited, whilst one the size of a hen's egg (Blackburn\*) was passed *per rectum* by an old woman without much difficulty. At times, however, the patient suffers a good deal of pain and distress from his attempts to void a gall-

\* Loc. cit.

stone *per anum*. A healthy adult farmer whom I saw, was almost in a state of collapse from his endeavours to pass a calculus, the size of a small pigeon's egg, which could easily be felt in the rectum, though it could not be removed by the finger. Enemata of water and warm olive oil were given, and the stone was finally passed whilst the patient was in an upright position, his previous attempts when lying down having been quite unsuccessful. He had once before experienced similar difficulty in passing a calculus, which was evidently the fellow to the one I saw. In this case the rectum contained no faecal matter, and this probably was the cause of the trouble, for much larger calculi may be expelled without any difficulty when accompanied by a large motion.

*The Size of Biliary Concretions which escape through the Bowel* without exciting any abdominal symptoms, varies greatly; but it is doubtful whether any of a greater diameter than 1 inch (2·5 cm.) can pass along the small intestine and through the ileo-cæcal valve with any degree of certainty. The large calculus mentioned previously which Blackburn described was  $3\frac{3}{8}$  inches (8·5 cm.) long by  $1\frac{1}{2}$  inches (3·75 cm.) broad, and this was passed *per rectum*, without exciting any symptoms until it reached the anus, when some little difficulty was experienced in its escape from the bowel. On the other hand, Hutchinson\* operated on a patient in whom obstruction of the bowel was caused by a stone  $3\frac{1}{2}$  inches (9·5 cm.) in

\* 'Brit. Med. Journ.,' Dec. 7th, 1895.

circumference, about the size of a Murphy's intestinal anastomosis button.

It not infrequently happens, then, that a calculus which escapes from the biliary passages by a biliary-intestinal, and especially by a gall-bladder-duodenal fistula, is too large to be able to pass along the small intestine or through the ileo-cæcal valve, and it becomes impacted in the bowel and causes obstruction to the onward movement of the intestinal contents, changes in the wall of the bowel at the seat of impaction, and local peritonitis.

The above conditions which a gall-stone in the intestinal tract may set up are most important, for their consequences are very serious, and over half the cases of intestinal obstruction from gall-stones terminate fatally.

*The Frequency of the Occurrence of Intestinal Obstruction from Gall-stones* is fortunately not great in England. Only one case has occurred at the Manchester Royal Infirmary since 1883, and probably since an earlier date. The total number of *post-mortem* examinations made in this hospital since 1881 is 2385, and evidence of intestinal obstruction from a gall-stone was met with in only the one instance referred to on page 198. Since 1883 about 50,000 in-patients have been treated in the hospital.

Mayo Robson found from inquiries at various hospitals, that four cases of the affection were treated in twelve months, during which time the wants of over 80,000 patients were attended to.

### Varieties of Intestinal Obstruction from Gall-stones.

The usually accepted form of intestinal obstruction from gall-stones—namely, that arising from the impaction of a calculus in the gut—is, according to Mayo Robson,\* only one of four varieties of obstruction which depend on this cause. He proposes to classify these four varieties as follows :

(1.) The form depending on *local peritonitis, excited by an inflamed gall-bladder, leading to paralysis of the bowel*. These cases may yield to general treatment without operation. The symptoms which indicate this form of intestinal obstruction from gall-stones are : a previous history of similar attacks, with biliary colic and jaundice ; severe and persistent pain, at first localised in the right side only, and then becoming general ; the late onset of faecal vomiting after continual retching ; the existence of collapse in an early stage from the severity of the pain, which is usually relieved by morphia ; and the onset of jaundice if the concretion, which remains in the biliary passages, have reached the common duct.

Von Winiwater described a case in which a calculus in ulcerating out of the gall-bladder broke into two. One half passed into the intestine, and causing obstruction was removed by operation, whilst the second half remained in the fistulous track between the bowel and the gall-bladder and set up fatal peritonitis (quoted by Eve†).

\* ‘ Med.-Chir. Trans.,’ Lond., 1895.

† ‘ Brit. Med. Journ.,’ Jan. 26th, 1895.

Lane\* operated upon a case of acute intestinal obstruction which was set up by paralysis of the colon from the formation on it of lymph at the hepatic flexure where it was in contact with a gall-bladder in an empyematous condition. The cause of the cholecystitis was not found out, but no stones were discovered in the gall-bladder. The case recovered after removal of the lymph from the colon and drainage of the gall-bladder.

(2.) *Volvulus of the Small Intestine* occurs as a complication of cholelithiasis at times, and is dependent either on the violence of the colic caused by an attack of cholelithiasis or on the contortions induced by the passage of a large concretion through the small intestine. In two such cases Mayo Robson performed laparotomy and untwisted the volvulus, recovery following in each instance. He considers that operation holds out the only hope of success in these cases. A positive diagnosis of the condition is, as a rule, impossible until the abdomen be opened. In both the above cases, in addition to the usual signs of acute intestinal obstruction, there was a well-marked localised swelling near the umbilicus, becoming hard at intervals when the paroxysms came on, and pointing to the situation of the obstruction.

(3.) *Mechanical Obstruction* due to the passage through the intestine of a large concretion. This is the most important variety, and will be referred to in detail immediately.

(4.) *Obstruction depending on Adhesions or Stricture of the Bowel*, the result of past gall-stone attacks, or

\* 'Lancet,' Feb. 25th, 1893.

of healing fistulæ. The symptoms of subacute or chronic partial intestinal obstruction are generally present in these cases.

### Intestinal Obstruction from the Impaction of a Gall-stone in the Lumen of the Bowel.

This, the third of Mayo Robson's four varieties, is the commonest and most important form of intestinal obstruction from gall-stones, and is the condition generally referred to when this complication of cholelithiasis is mentioned. Most of the further observations on this subject will therefore bear on the impaction of biliary calculi in the lumen of the gut.

*Age of the Patients.*—From the frequency of the occurrence of biliary calculi in old women, it is not surprising to find that they become impacted in the intestinal tract of the same class of subjects more often than in any other class.

Schüller\* found that men were affected in only 25·9 per cent. of 139 published cases.

The relative frequency of the affection in the various periods of life is as follows (Schüller).

Under 30 years	. . .	4
Between 31 and 40	„ . . .	5
„ 41 „ 50	„ . . .	17
„ 51 „ 60	„ . . .	33
„ 61 „ 70	„ . . .	29
„ 71 „ 80	„ . . .	16
„ 81 „ 90	„ . . .	3
Over 90	„ . . .	1

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\* “Gallensteine als Ursache der Darmobstruktion.” Doctor-Dissertation, Strassburg, 1891.

The youngest of the above patients was eighteen, and the oldest ninety-four.

About 75 per cent. of the above cases occurred in patients over fifty years of age. The possibility of intestinal obstruction being due to this cause must therefore be seriously considered in diagnosing indistinct obstructive intestinal conditions in old people, and especially in old women.

*The Length of Time during which a Calculus may remain in the Bowel* varies from a few days to fifteen years. Eve\* recorded a case in which the calculus probably remained in the small intestine for ten years without exciting any symptoms more serious than slight constipation until it reached the ileo-cæcal valve, when complete obstruction came on.

Smith† published a case of a calculus escaping from the biliary passages fifteen years before it finally caused obstruction of the bowel. During this time constipation with unformed motions was the only symptom of which the patient complained.

Courvoisier‡ refers to a case (No. 1011) in which twenty-two calculi were found in a curious diverticulum of the duodenum in a woman of eighty years of age, and which had caused all sorts of unpleasant symptoms during life. It is not stated how long they had been in this situation. As a rule the calculus only remains from a few days to a few weeks in the alimentary tract before setting up serious symptoms of obstruction.

\* 'Clin. Soc. Trans.,' 1895.

† 'Lancet,' Dec. 3rd, 1887.

‡ Op. cit.

*Situation of the Obstruction.*—The following table (Courvoisier)\* shows the portions of the intestinal tract in which biliary calculi are most frequently impacted.

	Leichtenstern.	Courvoisier.
Duodenum . . . . .		3
Jejunum . . . . .	10	4
Upper part of small intestine		1
„ „ ileum . . . . .	—	4
Middle „ „ . . . . .	5	1
Ileum . . . . .	—	18
Lower part of ileum . . . . .	17	10
Ileo-cæcal valve . . . . .	—	7
Vermiform appendix . . . . .	—	2
Sigmoid flexure of colon . . . . .	—	2
	32	52

The large calculi which cause intestinal obstruction as a rule escape from the biliary passages by a fistulous communication between the gall-bladder and the bowel. They rarely pass down the common bile-duct. Courvoisier could only find three undoubted instances of the obstructing calculus having escaped by the latter channel out of thirty-six cases recorded.

The higher up in the intestine the biliary fistula occurs, the more danger is there to the patient, and calculi which enter the bowel through an opening in the wall of the colon have a much more likely chance of escaping from the body than those have which must travel down the small intestine and through the ileo-cæcal valve.

Calculi are not uncommonly found obstructing the latter valve-opening itself, and they also frequently

\* Op. cit., p. 104.

lodge about eighteen to twenty-four inches above it in the ileum.

Occasionally a fatal obstruction of the colon may result after the calculus has entered it through a fistulous opening in its wall. Morison\* operated on a woman and removed an obstructing gall-stone from the sigmoid flexure. The patient died.

When gall-stones have remained some time in the intestinal tract they not uncommonly increase in size from the deposition of fæcal matter on them; and the obstructing concretion may consist of a conglomeration of several small calculi united together by a pasty material.

The *duration* of the obstruction may vary from one to twenty-eight days, but is not often more than fourteen days. About 87 per cent. of the cases terminate either in death or relief of the obstruction in fourteen days, and 70 per cent. in the first ten days.

Sargent† published the case of a woman, æt. 35, who died suddenly in less than half an hour after being taken "violently ill." She had previously suffered from "dyspepsia" only, and there had been no jaundice or any other symptoms of cholelithiasis. A *post-mortem* examination of the case was made, and in the small intestine was found a gall-stone  $1\frac{3}{4}$  inches (4.5 em.) long by  $\frac{3}{4}$  inch (1.75 em.) thick. The concretion completely filled the lumen of the bowel, and the wall of the intestine was tightly stretched over it. The latter was healthy above and below the obstruction, and "almost so" over the stone. There was no sign of peritonitis. A gall-bladder-duodenal fistula was present, through which the concretion had entered the intestine. It was thought that the patient had died from the severity of the pain which accompanied the fatal illness.

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\* 'Edin. Med. Journ.,' 1888.

† 'Brit. Med. Journ.,' 1879, vol. i, p. 852.

*Prognosis.*—The mortality varies according to different authorities (Naunyn\*) :

Schüller collected	82	published cases,	of which	56	per cent.	died.
Dufort	„	73	„	„	„	56 „ „
Courvoisier	„	125	„	„	„	44 „ „

Operative treatment does not seem to increase the chances of recovery. Up to the end of 1891 Naunyn found that only two of thirteen cases operated upon recovered. Eve traced nine recoveries out of eighteen operation cases, and J. Hutchinson, Senior,† who has for some years been engaged in amassing evidence on this point, has come to the conclusion that the mortality of cases treated surgically is a little over 50 per cent., and he considers that the question of operative interference for mechanical intestinal obstruction from gall-stones is still *sub judice*. It is certain that many very severe cases recover with medical treatment only.

*Recurrent Attacks of the Obstruction.*—Patients occasionally recover from one attack of intestinal obstruction only to undergo another, or even two or three more attacks, each brought on by the passage of large gall-stones through the small intestine and the ileo-cæcal valve. Maclagan‡ met with two such cases.

The first patient was a woman æt. 63, who, previous to coming under Maclagan's observation, had suffered from four attacks of intestinal obstruction during the space of less than two months. The first two attacks lasted six days, the third four, and the fourth five days, during each of which there was vomiting of the contents of the stomach and

\* Op. cit., p. 149.

† 'Brit. Med. Journ.,' 1895, p. 195.

‡ 'Clin. Soc. Trans.,' vol. xxi, p. 87.

small intestine, acute abdominal pain, and absolute constipation. Twelve days after the last attack she passed *per anum* four large gall-stones, each of which was nearly one inch in diameter. The patient improved for a time after these attacks, but about two months before MacLagan saw her she had suffered from another similar but more severe attack, lasting a longer time and followed by the passage *per anum* of a gall-stone like the others. No improvement, however, took place in the general condition of the patient, and she died about one month after the cessation of the last attack of obstruction. A *post-mortem* examination was made, and a fistulous passage between the gall-bladder and duodenum was found. There were some patches of lymph on the peritoneal surface of the bowel. Only remains of the folds of the ilco-cæcal valve were present, the valve having probably been destroyed during the passage of the first gall-stone.

The second case was also a woman, æt. 60, who complained of severe abdominal pain coming on about one hour after food. A tumour the size of a hen's egg was found in the region of the gall-bladder, which was tender when pressed upon, the pain so caused being like that which came on after food. The tumour was evidently connected with the gall-bladder. She remained in the same condition for some weeks, when she was suddenly seized with symptoms of intestinal obstruction, and the gall-bladder swelling was found to have diminished to the size of a pigeon's egg. No stool was passed for twenty-three days, and during the last ten days no flatus escaped. The symptoms were finally relieved, probably by the escape of the concretion through the ileo-cæcal valve into the colon, and the patient improved steadily for ten weeks. At the end of this time she was again seized with sudden symptoms like those of the first attack, and the swelling in the region of the gall-bladder could scarcely be felt at all. The condition gradually got worse, and patient died in about four weeks. Tympanites was a marked symptom in both attacks. During the period of improvement after the first attack a distinct lump like a walnut or big gland could be felt in the right side near the crest of the ilium, which was supposed to be a gall-stone. No *post-mortem* was made on this case.

The diagnosis of obstruction from gall-stones was made during life in both patients. MacLagan thought that death was caused in the two cases by inflammatory disturbance in and around the liver, set up by the entrance into the gall-bladder of the contents of the intestine.

A calculus forming half a complete cast of a gall-

bladder may be passed *per anum* without difficulty, whilst its fellow-half will cause obstruction. Clutton\* describes such a case.

A woman, æt. 76, passed a large gall-stone *per anum* with symptoms of cholelithiasis, including jaundice. After these symptoms had subsided, a tumour could be felt in the position of the gall-bladder, but the patient remained well for fifteen months, when she was suddenly seized with severe abdominal pain, vomiting, and other symptoms of acute intestinal obstruction. The tumour in the region of the gall-bladder was found on examination to have vanished, and the true cause of the obstruction was suspected. Laparotomy was performed, and a conical concretion was found about 8 inches from the lower end of the ileum, which was pushed on through the ileo-cæcal valve without much difficulty. Five days later it was passed *per anum* after some trouble with the rectum, and was found to consist of a gall-stone  $1\frac{1}{4}$  inches (3.1 cm.) long by 1 inch (2.5 cm.) broad, and  $3\frac{3}{10}$  inches (8.25 cm.) in circumference. It had one large facet which fitted to that on the calculus passed fifteen months previously.

The successful result in this case was due mostly to the fact that the operation was undertaken only twenty-four hours after the onset of the acute symptoms, by which time the gut round the stone had hardly had time to become much injured. The manipulation of the stone was also rendered more easy by its narrower end lying nearer the valve than the broad end.

**Gall-stones in the Vermiform Appendix.**—A small biliary concretion may get into the vermiform appendix and cause perityphlitis. This probably happened in a case which Thorowgood† has recorded. An abscess developed in the right iliac region in a girl aged 10, who had often suffered from bilious attacks and vomiting. This abscess was opened, and from it a concretion about the size of a small nutmeg escaped. The child recovered. The calculus was analysed, and found to consist chiefly of cholesterin.

\* 'Clin. Soc. Trans.,' vol. xxi, p. 99.

† 'Trans. Path. Soc. Lond.,' 1877, p. 131.

Fauconneau-Dufrésne\* refers to a case of Wegeler's in which a patient died from symptoms of intestinal obstruction, and *post-mortem* the lower part of the ileum and the cæcum were inflamed and gangrenous. The gangrene started from the vermiform appendix. The latter structure was distended, and contained several gall-stones, one the size of a pigeon's egg.

**Biliary Calculi in the Colon or Rectum.**—When once a gall-stone has passed into the large intestine, as a rule no further trouble need be expected from it; but not a few cases, however, are recorded in which a large biliary concretion has set up obstruction in the colon or rectum, and has even caused death.

Fiedler† refers to a case in which vague pains in the region of the stomach, unaccompanied by jaundice or any symptoms typical of biliary colic, were followed after two months' interval by pain in the epigastrium, then in the right lumbar region, and finally over the sigmoid flexure. Vomiting was frequent, and the left thigh was drawn up to the abdomen owing to severe pain in the left iliac region, where a tumour could be felt. After a further period of two months, a concretion consisting of three faceted stones weighing 46 grammes and composed of 96 per cent. of cholesterin, was passed, with consequent relief of the symptoms and disappearance of the tumour.

Morison‡ and Körte§ each removed a large gall-stone

\* Ref. Schüller, *op. cit.*, p. 32.

† Ref. Schüller, *op. cit.*, p. 31.

‡ 'Edin. Med. Journ.,' 1888.

§ Ref. Eve, 'Trans. Clin. Soc. Lond.,' 1895, p. 91.

by laparotomy from the sigmoid flexure of a woman. The latter case recovered, but Morison's died.

Pye-Smith\* examined *per rectum* a case of intestinal obstruction, and felt something abnormal above the sigmoid flexures which was very moveable and which was looked upon as being possibly a cancerous growth. A large biliary calculus was passed in thirteen days *per rectum*, and the obstruction was relieved.

Schüller† mentions four cases (all women) in which palpation of the abdomen was followed by relief of the symptoms and by the passage, a short time afterwards, of an obstructing calculus. In three of the cases there had been fæcal vomiting. Two of the patients stated that they felt something move inside them at the time of the examination.

Dr. Dreschfeld told me of a case of intestinal obstruction in which he made a digital examination of the rectum, and found a gall-stone lodged in a syphilitic stricture of this organ. He managed to remove the stone with his finger, and the obstruction was relieved.

### The Symptoms of Intestinal Obstruction from Gall-stones.

The symptoms excited by the impaction of a gall-stone in the intestinal tract are very similar to those resulting from intestinal obstruction which is due to other causes. It is, as a rule, impossible to diagnose the former condition, and very often the first definite indication of the true cause of the

\* 'Lancet,' 1887, i, p. 573.

† Op. cit., pp. 10 and 12.

obstruction is obtained during the operation undertaken for the relief of the condition.

A previous history pointing to the escape of gall-stones from the biliary passages is of much diagnostic value. Out of about forty cases of intestinal obstruction from gall-stones, in which reliable information could be obtained from the patient, Naunyn \* found that previous symptoms of cholelithiasis had been present in twenty-six instances. A reliable history concerning the occurrence of jaundice was obtained by Naunyn in forty-two cases of the same affection. Sixteen of these patients stated that they had been jaundiced on previous occasions, whilst twenty-six stated definitely that their skin had never been discoloured. The same observer found, from the history of 120 cases of intestinal obstruction from gall-stones, that symptoms caused by the escape of the calculus into the intestinal tract from the biliary passages were observed in forty-one instances.

In favorable cases the obstructing concretion may be felt through the abdominal wall, as in the case recorded by Jeaffreson,† but more frequently this is impossible, owing to the presence of tympanites. Eve‡ felt a mass like a rifle bullet in the right iliac region of a patient after the administration of an anæsthetic, which he could not feel before.

It is not always easy to recognise a large gall-stone in the abdominal organs even during laparotomy,

\* Op. cit., p. 145.

† 'Brit. Med. Journ.,' May 30th, 1868.

‡ 'Trans. Clin. Soc. Lond.,' 1895, p. 91.

as is seen in Godlee's\* case, in which he cut down on an obscure tumour in the lumbar region. To get at the tumour he had to break down adhesions between the transverse colon and the liver, and in doing this he came across two hard masses, one in the gall-bladder and one in connection with the liver. He concluded that these were malignant tumours, but some time afterwards, the woman passed a large gall-stone, and the tumour disappeared.

*Tympanites* is not always present, and is often but slightly marked. It tends to develop if the obstruction persist for some time, and especially if it be low down in the ileum. When the obstruction is high up in the jejunum or duodenum, the epigastric region is distended, whilst the rest of the abdomen is retracted.

*Vomiting* is an important symptom. It is often the first, but it varies greatly in its intensity and frequency. When the obstruction is high up in the jejunum or in the duodenum, the vomiting is usually bilious and not faecal, but when lower down in the ileum the vomited matters become faeculent. In a few cases jejunal obstruction may result in the vomiting of brownish semi-faecal matter. Occasionally there is hæmatemesis, the blood escaping from the edges of a recent fistulous communication between the intestine and the biliary passages. The higher up in the bowel the obstruction, the more severe, as a rule, is the vomiting. In a case of Pye-Smith's† where the stone was impacted thirty inches below the pylorus, five litres of bilious fluid were vomited in forty-eight

\* 'Brit. Med. Journ.,' March 2nd, 1895.

† 'Trans. Path. Soc. Lond.,' vol. v, p. 163.

hours. When the pylorus is affected, the vomiting is profuse, and dilation of the stomach ensues.

In all patients over fifty, and especially in women above this age, the possibility of a gall-stone causing intestinal obstruction must be remembered.

The symptoms of obstruction may also be *intermittent*. This generally happens when the gall-stone is not big enough to completely fill the lumen of the bowel, but by its presence excites spasm of the wall of the intestine, which then grips the stone and holds it fast. Whilst this spasm continues the symptoms of complete obstruction are present, but as soon as the muscle in the wall of the bowel becomes paralysed by over-exertion and relaxes, the contents of the intestine can pass by the stone, and the urgent symptoms are relieved, although fæcal vomiting may continue whilst fæcal matter is being passed *per rectum*. Naunyn\* is of the opinion that flatus is more regularly and persistently passed when the intestinal obstruction is due to a gall-stone than when it is due to other causes, and that it may occur when there is complete fæcal obstruction from the former cause. Diarrhœa is occasionally present for a considerable time, as in a case of Barker's,† in which a gall-stone was impacted in the ileum just above the ileo-cæcal valve.

#### Diagnosis of the Situation of the Obstructing Stone.

The symptoms of intestinal obstruction from a gall-stone vary in some rather important points ac-

\* Op. cit., p. 146.

† 'Brit. Med. Journ.,' 1895, i, p. 195.

according to the portion of the alimentary tract in which the stone is lying.

(1.) *Pylorus*.—Though obstruction of the outlet of the stomach can hardly be looked upon as a form of intestinal obstruction, it will be worth while to consider its chief symptoms here for the sake of comparison with those excited by the real affection. In obstruction of the pylorus there are frequent vomiting or retching, occasional hæmatemesis, and gastric dilatation. The bowels act fairly well, as the obstruction is generally only partial. There may be epigastric fulness, but the lower part of the abdomen is retracted. If the obstruction be due to the formation of a biliary-gastric fistula, bile may be present in the vomited matters.

(2.) *Duodenum*.—The symptoms of obstruction of the duodenum are similar to those arising from stenosis of the pyloric orifice, but gastric dilatation is not present, and there is complete stoppage of the bowels after a few days. Bile is vomited in considerable quantity.

(3.) *Upper Part of the Jejunum*.—The vomiting is very frequent and profuse, and the fluid brought up is beginning to be fæculent. The epigastrium is tympanitic, and the abdomen in other parts retracted.

(4.) *Ileum*.—The vomiting becomes quite fæcal, and there is rapid onset of complete fæcal obstruction. The umbilical and hypogastric regions of the abdomen become tympanitic, whilst the collapsed large intestine occupies the flanks. A hard foreign body felt through the abdominal wall in the right iliac

region is very likely to be a gall-stone impacted in the ileo-cæcal valve.

(5.) *Colon*.—When the stone is blocking up the colon the symptoms develop more gradually than when it is in the small intestine. The vomiting comes on later, but the fæcal obstruction is complete from the beginning; generally tympanites develops, and becomes very marked in time. A rectal examination by the finger may reveal the presence of the obstructing stone when it is in the sigmoid flexure or rectum.

Attempts to localise the position in the intestines of an impacted gall-stone by sounding with a long thin needle passed through the abdominal wall, ought not to be made. Good results can very rarely follow from such a procedure, and the viscera may easily be seriously injured by the multiple punctures to which they are subjected by its adoption. The contents of distended intestines are also very liable to pass out through the punctures into the cavity of the abdomen and excite general peritonitis.

An exploratory laparotomy, developing into any operation necessary for the relief of the condition which is found to be the cause of the symptoms, is the safer procedure to adopt.

### Perforation of the Intestine.

A gall-stone in the intestine may, in addition to causing obstruction, perforate the wall of the bowel. Jeaffreson\* relates such a case :

\* 'Brit. Med. Journ.,' May 30th, 1868.

The patient, a woman æt. 53, complained of griping abdominal pain, and on examination, a hard body, the size of a walnut and like an enlarged gland, was felt lying midway between the umbilicus and the right iliac fossa. It was not felt at a subsequent examination, and was not suspected of being a gall-stone, as there had been no history of biliary colic. The patient was shortly afterwards seized with sudden severe abdominal pain, collapsed, and died in thirty-six hours. *Post-mortem*, general peritonitis, especially marked in the right iliac fossa, was found. The duodenum was adherent to the fundus of the gall-bladder, although no actual perforation existed in the adherent tissues. The gall-bladder contained calculi. The ileum was found to be perforated just above the ileo-cæcal valve, and a large gall-stone was lying in the peritoneal cavity of the pelvis.

### Stricture of the Intestine.

Stricture of the intestine occasionally results from the irritation of gall-stones. In a case of Ward's\* chronic inflammation and thickening of the ileum and cæcum, close to the valve, with practical destruction of the ileo-cæcal valve itself, was found. The mucous membrane in these situations was eroded away by ulceration, and large faceted gall-stones were found in the thickened portion of the bowel. The ileum again, three feet above the valve, contained another large oval biliary concretion. The wall of the bowel round the obstruction was thickened, and below it the lumen of the intestine was much narrowed. This patient had for three years suffered from chronic diarrhœa with occasional attacks of vomiting and severe abdominal pain. There were no symptoms of biliary colic.

\* 'Traus. Path. Soc. Lond.,' 1852.

## CHAPTER XII.

Complications and Sequelæ of Cholelithiasis, continued—Cancer of the Biliary Passages—Hydrops Cystidis Felleæ—Interstitial Pancreatitis—Calculous Cirrhosis of the Liver—Glycosuria.

**Carcinoma of the Biliary Passages.**

THE question as to whether cancer of the bile-ducts or gall-bladder is a cause or result of the formation of gall-stones was fully discussed in Chapter III (page 56), and it was shown that the malignant growth very frequently develops after gall-stones have been present in the biliary passages. It is not necessary to go into the subject again, but a few of the important points connected with it will not be out of place here.

*Primary Carcinoma of the Bile-ducts*, according to Rolleston,\* consists in the majority of cases of cylindrical-celled growths, but when the disease invades the ducts by extension from the gall-bladder, it is more of a columnar-celled type.

*Symptoms.*—The onset of cancer of the bile-ducts is, almost without exception, marked by the development of jaundice. The discoloration of the skin gets progressively worse, and often assumes a dark olive tint. It never improves. The cachexia of cancer develops rapidly in the course of a few weeks.

\* 'Manchester Med. Chron.,' January, 1896.

The diagnosis of cancer of the bile-ducts in the early stages of the affection is often impossible. The development and progressive increase of the jaundice is a most important indication of the disease. As a rule, a probable diagnosis can only be made after observing the progress of the case, and by the onset of marked cachexia, but even this latter condition may be present in obstruction from non-malignant causes. The true nature of the case may not be discovered until a *post-mortem* examination be made.

*Primary Carcinoma of the Gall-bladder* consists, according to Rolleston,\* of a columnar-celled or, less commonly, of a spheroidal-celled growth.

*Symptoms.*—Jaundice is absent so long as the growth remains limited to the gall-bladder, and there is no pressure on the hepatic or common duct. This symptom is therefore not essential for the diagnosis of the disease, and when present is due, either to extension of the primary growth into the bile-duct, or to pressure exerted by it on the hepatic or common duct. It occurs in about 69 per cent. of the cases of cancer of the gall-bladder (Musser).†

The presence of a small, nodular or irregular, hard tumour can at times be made out. The enlargement of the gall-bladder is not so great in this condition as when it is dilated from obstructive causes, unless the growth involve the neck of the organ. A cancerous growth of the gall-bladder generally continues to enlarge, and does so rapidly enough for its increase in size to be noticeable. Cachexia develops

\* Loc. cit.

† Loc. cit.

in the course of two or three months. The occurrence of pyrexia and rigors is against the presence of new growths, though they do accompany it at times. Ascites is set up by extension of the growth to the glands in the fissure of the liver. The liver is rarely increased in size except as a result of obstruction of the common duct. The spleen is not enlarged. An exploratory puncture of the tumour may result in the recognition of cells of new growth in the fluid or material obtained in the needle.

### Hydrops Cystidis Felleæ.

This condition consists in the distension of the gall-bladder by clear, colourless fluid, which very frequently results from complete obstruction of the cystic duct by a gall-stone, or by compression or inflammatory causes. It develops most commonly when the duct is blocked by a stone either in the neck of the gall-bladder or in the lumen of the duct itself.

Courvoisier\* states that out of a total of ninety-one cases of distended gall-bladder resulting from a stone in the cystic duct the condition of *hydrops cystidis felleæ* was present seventy-nine times.

The fluid contained in the distended gall-bladder is clear and colourless, and consists in great part of mucin. It occasionally contains a little albumen or blood, or a few crystals of cholesterin, but no bile pigments or bile salts. A small quantity of organic salts may be present. The fluid is secreted by the mucous membrane, the epithelial cells of which are

\* Op. cit., p. 20.

more cubical than normal, and it is sterile. The tumour is often latent, only attracting attention from its size, but there is generally a previous history of biliary colic. For its development a complete obstruction of the cystic duct is necessary, otherwise bile would enter the gall-bladder. The physical signs of this condition, and the shapes assumed by the tumour, are similar to those described under "Distension of the Gall-bladder."

### Interstitial Pancreatitis.

Riedel \* has recently drawn attention to an enlargement of the head of the pancreas of an interstitial inflammatory nature which he has occasionally (three times in twelve cases of gall-stone surgery) met with as a result of cholelithiasis. Impaction of a calculus in the ostium duodenale of the common bile-duct seems greatly to favour the development of this condition. This latter duct frequently runs through the head of the pancreas to reach the duodenum, and often unites with the pancreatic duct before they reach their common duodenal orifice. Inflammation of the wall of the common bile-duct in such cases extends to the pancreatic duct or to the pancreatic tissue itself, and excites an inflammatory increase of the interstitial tissue which leads to the formation of "iron"-hard nodules. These nodules are at times mistaken by the examining finger, in cases of gall-stone surgery, for calculi in the duodenal end of the common bile-duct. More rarely the head of the pancreas is enlarged, in consequence of this inter-

\* 'Berl. klin. Woch.,' 1896, Nos. 1 and 2.

stitial inflammation, to form a distinct tumour, which has nearly all the characteristics of cancer, and in fact can only be diagnosed from it by the progress of the case after the removal of the exciting cause of the inflammation. This hypertrophic interstitial pancreatitis may be met with when calculi are found in the gall-bladder only, although it is very probable that one has previously been engaged in the duodenal end of the common duct. Of a benignant nature really, interstitial pancreatitis may, if left for long, induce a fatal cachexia as a result of obstruction to the escape of the bile and pancreatic juice. It runs a slow and protracted course if left alone. Riedel operated on three such cases with two recoveries and one death. The latter was due to the pancreatic cachexia having exhausted the vital energies of the patient.

### **Calculous Cirrhosis of the Liver.**

Cirrhosis of the liver occasionally develops in prolonged obstruction of the common bile-duct by a gall-stone. In writing in a previous chapter (p. 127) on the enlargement of the liver met with in cholelithiasis, the nature of the new tissue formed around the dilated bile-ducts was referred to, and it will hardly be necessary to go more fully into the same subject here, as cirrhosis of the liver is rarely, if ever, met with clinically as a complication of cholelithiasis.

The liver, as a rule, enlarges at first when the cirrhosis is developing, but if the case is prolonged sufficiently it assumes the atrophic form. This latter condition was present in four out of the forty-six

cases in which I found gall-stones *post-mortem*, but whether as a cause or result of the latter, could not be determined.

The development of the cirrhotic tissue takes place outside the duct-wall and at the expense of the liver cells, and is due partly to the prolonged irritation of the duct-wall by the retained bile, which results in a chronic hypertrophic angiocholitis, and partly to a hypertrophy of the wall of the duct which is set up to compensate for the atrophy resulting from its distension.

If a large liver be observed during life to diminish in size, whilst the jaundice and other symptoms of obstruction persist, the possibility of the development of an atrophic cirrhosis must be thought of.

Ascites is generally absent in cases of biliary cirrhosis, according to Chauffard,\* because the blood passes by a supplementary venous anastomosis from the branches of the portal vein in Glisson's capsule into the neighbouring branches of the sublobular hepatic vein.

### Glycosuria.

Several instances have been recorded in which sugar has been found in the urine in cases of gall-stones.

From the frequency of the occurrence of both conditions, especially in elderly and stout subjects, their association might be looked upon as a coincidence, but occasionally the glycosuria seems to be dependent upon the attacks of gall-stones.

\* Op. cit., p. 886.

Gans\* and Kraus† met with sugar in the urine regularly during, and after, the attacks of biliary colic, and Ord‡ published a case in which a patient suffered from thirst and glycosuria for some months, during which time he had several attacks of biliary colic. Treatment for cholelithiasis brought about the passage of a gall-stone *per anum*, after which the colic left him, and the symptoms of diabetes disappeared.

\* 'Verhandl. d. Cong. f. inner. Medicin,' 1891, p. 76.

† 'Prag. med. Woch.,' 1884, No. 49.

‡ 'Brit. Med. Journ.,' 1887, i, p. 497.

## CHAPTER XIII.

Medical Treatment of Cholelithiasis—Experimental Researches on Cholagogues—Medicinal, Hygienic, and Dietetic Treatment of Cholelithiasis—Medical Treatment of Intestinal Obstruction from Gall-stones.

GALL-STONES may be treated either medically or surgically. Medical treatment is adopted at the onset of all cases, and in the majority of instances is used throughout the course of the illness. In a large minority of cases, however, some complication develops in the course of the disease, for the relief of which the aid of the surgeon is necessary. The symptoms and conditions which call for surgical treatment will be referred to in later chapters, along with an account of the treatment itself. The measures employed by the physician for the relief of the disease will be considered first.

**Medical Treatment of Cholelithiasis.**

The results of the medicinal treatment of this disease, as of almost all other affections for which there is no specific remedy, vary greatly in different cases; very often, however, much relief to the patient, and not uncommonly a cure, may result from the employment of suitable medicinal measures. Most of the drugs which are of value at the present

time for the relief of the symptoms of gall-stones have been used with a varying amount of success during the last century and a half.

At the first glance it might appear from this statement that our knowledge of the medicinal treatment of cholelithiasis had not progressed much during this century, and this impression is emphasised by the admission of the fact that not one new remedy of any great value has been discovered since Coe's time (1750). But if the discovery of new remedies has failed, it must be remembered that the knowledge concerning the action of the old ones has increased greatly, and in consequence, although the treatment of gall-stones as carried out at the present time is very similar to that which was in vogue 150 years ago, it is now based upon firm scientific principles, whereas formerly it was used for empirical reasons only. And for the same scientific reasons we have omitted many reputed remedies of the last century which, from their very nature and physiological action, could be of no use in the cure of the disease. For instance, mineral waters have been for some time, and still are, ordered freely for patients suffering from gall-stones, with beneficial results, which were often attributed by the older physicians to the solution of the calculi. At the present time, however, we know that the various salts which are contained in the saline waters are all possessed of some cholagogue action, and that they improve the condition of the liver and alimentary tract generally, and thereby do away with a strong predisposing cause of the development or persistence of cholelithiasis.

And we also know that they do not dissolve gall-stones.

It is the same with our knowledge of the other drugs used in the treatment of gall-stones.

It will be interesting and instructive in this place to review briefly the most important results of experimental observations in man and in animals, with the different remedies used in the treatment of cholelithiasis.

### **Experimental Researches on Cholagogues.**

A good many observations have during recent years been made on the effect of various drugs in increasing the excretion of bile, both in man and in animals. Those made on man are the most important, but the results obtained are unsatisfactory at the best of times, for the amount of bile excreted, estimated by volume or by its solid residue, varies greatly from day to day in the same subject. Thus Noël Paton and Balfour\* found that their patient normally excreted from 518 c.cm. to 814 c.cm. of bile, and that the solids varied from 7·9 grms. to 11·5 grms. daily. In Mayo Robson's case similar fluctuations were observed normally.

The conclusions to which Noël Paton and Balfour have been led from their observations on the effect of diet and drugs on the excretion of the bile in a woman, are as follows :

(1) The meals usually taken appear to have no immediate effect on the flow of bile or on the amount of solids contained in the bile.

\* 'Lab. Rep. R. Col. Phys., Ed.,' vol. iii.

(2) The amount of fluid taken has a notable effect in increasing the flow of bile.

(3) Various drugs seem to influence the bile flow, and of these salicylate of soda and calomel appear to be active, ox-bile less markedly so.

Mayo Robson's conclusions\* from similar observations are as follows:

(1) The excretion of the bile is apparently not materially influenced by the diet.

(2) Calomel, euonymin, rhubarb, podophyllin, and benzoate of soda seemed rather to diminish, than increase, the amount of bile excreted. But slightly better results were obtained with turpentine and iridin. Soda-water, aerated, was given, and produced an increased flow in two hours' time. (How much of this increased flow was due to the water?)

In experimenting on dogs with biliary fistulæ the same irregularity of the normal flow of bile exists, and obscures the investigation of the influence of drugs on its excretion. The quantity varies from 8·8 to 21·1 c.cm. for each kilogram of the dog's weight per day (Stadelmann†).

From experiments on fasting, curarised dogs, Rutherford‡ comes to the conclusion that the following drugs are powerful hepatic stimulants:—Sodium phosphate, colchicum, jalap, colocynth, mercuric chloride, ipecacuanha, aloes, sodium benzoate, and sodium salicylate. The first four are powerful intestinal as well as hepatic stimulants. Ipecacuanha,

\* 'On Gall-stones,' 1892, pp. 33 and 34.

† Ref. Gumprecht, 'Deutsch. med. Woch.,' 1895, No. 17.

‡ Ref. Gamgee, op. cit., pp. 370—374.

sodium benzoate, and sodium salicylate are examples of hepatic stimulants almost without action on the intestinal glands.

Rhubarb and dilute nitro-hydrochloric acid are hepatic stimulants, though their action is much feeblar than that of those first referred to.

Calomel stimulates the intestinal glands but not the liver, whilst mercuric chloride has the opposite effect in medicinal doses.

Purgation produced by purely intestinal stimulants, such as magnesium sulphate, gamboge, and castor oil, diminishes the secretion of bile. When a substance, *e.g.* podophyllin, which powerfully stimulates the intestine as well as the liver, is given in too large doses the bile secretion may never be increased. Rutherford also found that bile is a cholagogue.

Since Rutherford's work, Rosenberg\* has found that olive oil, bile and sodium salicylate, are distinct cholagogues in dogs with permanent biliary fistulæ.

Pachkis, Nissen, and Baldi,† however, found that with the exception of bile itself, no agent introduced into the stomach or intestine of dogs with a biliary fistula affected the secretion of bile.

Stadelmann‡ holds that bile-salts, especially the glycocholate of soda, certainly increase the solid and fluid constituents of the bile in dogs.

Gamgee§ considers that the investigation of cholagogues is most difficult, for the various methods of research which have been employed are all more or

\* 'Pflug. Archiv,' xlvi, pp. 334—366.

† Ref. Gamgee, *op. cit.*

‡ 'Berl. klin. Woch.,' 1896, Nos. 9 and 10.

§ *Op. cit.* p. 371.

less open to objections which compel the utmost caution in drawing inferences from them, and have led to the above most contradictory results.

Such contrary experimental results are of little, if any, value to the physician, and, indeed, the methods adopted at the present time for the relief of cholelithiasis are almost entirely the result of clinical experience gained during the present and the last centuries in the treatment of the disease.

Before considering the various therapeutic, hygienic, and dietetic measures used at the present day it will be interesting to refer to the general medical treatment of the disease as carried out in the last century by Coe and other physicians.

In 1757, Coe\* recommended the following drugs as useful in relieving the symptoms of cholelithiasis: calomel, opium, oil of sweet almonds, soap in large quantities, mineral waters (Spa, Pymont, and Bath), &c. He further insisted upon the importance of exercise, on foot or on horseback, and if the patient could not afford a real live horse he was to make (according to the instructions given by Coe) a dummy or chamber-horse, and use that in his room at home. Abdominal massage, especially over the right hypochondrium, was, in Coe's opinion, well worth trying several times a day, and finally, if all the above means failed, an incision might be made into the gall-bladder and the calculi be extracted through that. Such an operation, however, was only to be undertaken when there was an adhesion of the distended

\* Op. cit.

gall-bladder to the peritoneum, otherwise the bile would flow into the cavity of the abdomen and lead to a fatal event.

It will be seen, then, that the medical treatment of cholelithiasis has not altered much during the last 150 years, but with the great advance made by general surgery during the latter half of this century, and by abdominal surgery in particular in the last decade, the prognosis of many cases which cannot be relieved by medicinal treatment, but which are suitable for operation, is greatly improved.

### **The Medicinal Treatment of Cholelithiasis.**

Medicinal treatment may be called for in cholelithiasis for the relief of the symptoms of the acute attacks, and for those excited after the subsidence of the acute condition, generally by the presence of one or more stones in the biliary passages, but not infrequently by the onset of some complication. In the following pages, however, the various symptoms will not receive individual attention, but they will be referred to in the consideration of those drugs which are held to be specially efficacious in their relief.

There is, unfortunately, no specific remedy for the disease, and many observers doubt whether calculi in the biliary system can be dissolved by any medicinal substances. It is true that gall-stones are dissolved by several drugs in the laboratory, and would be acted upon by them in the biliary system, were the latter excreted in sufficient quantity in the bile. But although it is unfortunately impossible to effect this with the majority of the remedies for gall-stones

as far as is known, it is not improbable that the good effect of oil and soap on the course of the disease depends to a certain extent on the excretion of these substances in sufficiently large quantity in the bile to exert a distinct solvent action on the calculi. This is a point, however, which will be referred to more fully later on.

The various drugs used in the relief of gall-stones will now be considered, and the hygienic and dietetic measures which are essential aids to the therapeutic treatment will be referred to afterwards.

*Water* increases the volume of the bile excreted, but probably has no effect on the amount of the solids present. It certainly is of practical use when given warm or hot and in large quantities (10—20 oz.). The pain of biliary colic is frequently relieved by its administration by the mouth, and the effect is increased by the addition of 20 or 30 grains of bicarbonate of soda to the pint. It acts in this way as a warm fomentation applied internally to the liver.

The quantity of water drunk daily during the routine treatment of the disease at one of the spas is an important element in the success of the cure.

*Alkalies*, especially in the form of *mineral waters*, have for a couple of centuries been considered to be of much use in the treatment of cholelithiasis. Their value is greater in the stages between the acute attacks of colic, although Kocher\* considers that Carlsbad salts in hot water often relieve the pain of gall-stones. For a long time their beneficial effect was attributed by some writers to the supposed power

\* Ref. Gumprecht, 'Deut. med. Woch.,' 1895, No. 17.

of the alkalies of dissolving the stones in the biliary passages, but at the present day the treatment is carried out more with a view to obtaining the good general effect which the alkalies undoubtedly have on the system, than with any hope of causing the solution of the calculi in the biliary passages.

As I could find no account of any experiments made to investigate the supposed solvent action of the alkaline salts on gall-stones, I myself carried out, in 1892, a series of observations bearing on the point, the results of which formed the basis for my "Dissertation for the Degree of Doctor of Medicine."\*

As a result of these experiments I found that the alkaline salts which occur in the various mineral springs, even when in strong solution in water, have not the slightest solvent action on a gall-stone. I kept gall-stones in solutions of the salts of various strengths, maintained at the body temperature, for periods of time varying from two to four weeks without there being any loss in the weight of the calculi at the end of the time.

The action of a solvent in the bile on a stone lying in the gall-bladder or bile-ducts is of course greatly aided by the movements of the bile about the stone, which result from the periodical contraction of the muscle fibres in the wall of the biliary passages. I endeavoured, therefore, in my experiments in the laboratory to imitate as nearly as possible the conditions under which a stone in the periodically emptying gall-bladder is acted upon by solvents in

\* Recorded in the Dissertation and in the 'Man. Med. Chron.,' Nov. and Dec., 1893.

the bile. For this purpose I devised an artificial gall-bladder, which consisted of a wide-mouthed, glass bottle holding two ounces of fluid, with an inlet thistle tube, a vent tube for the escape of air, and an automatically acting outlet syphon tube. The gall-stone was placed in the bottle, and the fluid containing the drug with which I was experimenting was allowed, drop by drop, to enter through the thistle tube. This went on for about three hours until the bottle was full, and then the outlet syphon tube acted automatically, and emptied in half a minute the fluid contents of the bottle. The latter then filled again slowly, was emptied, and so on for days together. The whole apparatus was kept at the body heat in an incubator. By this means I gave the supposed solvents of gall-stones the benefit of the aid derived from the physical erosion of the latter by a liquid moving over them, and yet could not find any loss in weight of the gall-stone. I have described more fully in my Graduation Thesis the above apparatus, and the results obtained with it.

Most physicians at the present time consider that the beneficial results which follow on the use of alkalies in cholelithiasis are due to the good effect which these medicines have on the system generally, but especially upon the liver and alimentary tract, an effect which is gained in great part by the daily evacuation of the bowels brought about when the salts are taken in sufficient quantity to produce such a result without purging the patient. The large volume of water in which the salts are administered, taken as

it is, as a rule, on an empty stomach, before a meal, plays an important part in bringing about the improvement in the patient's condition, for, in addition to aiding the aperient action of the salts, it dilutes the bile and increases the amount of urine. This latter action, by which the kidneys are "flushed" frequently, is desirable in the subjects of cholelithiasis, for they generally suffer from urinary lithæmia at the same time.

The supposed cholagogue action of alkalies is, I believe, entirely due to two causes: firstly, that by exerting an aperient action on the bowel they sweep out the bile contained therein, and create a demand for more; and secondly, the amount of water in which they are taken liquefies, and therefore increases in quantity (by volume), the bile excreted by the liver. The good effect obtained by the use of alkalies or mineral waters in cholelithiasis is similar to their action in gout, and is, to my mind, rather in favour of the theory that these affections are closely allied, and that the same hepatic derangement may be the cause of both.

Various *mineral waters* are held in great repute in the treatment of gall-stones. Of the Continental spas Carlsbad is the most popular. The waters there contain chiefly the sulphate, carbonate, and chloride of sodium, and the sulphate of potassium.

A course of Carlsbad waters undoubtedly does good in many cases, especially of protracted impaction of calculi, diminishing the severity of the general symptoms, and not uncommonly curing the patient. One Carlsbad physician asserts that you could pave half

the floor of the pump-house with gall-stones passed by patients whilst taking the waters there.

Contrexéville or Vittel in the Vosges district, Homburg, Kissingen, Vichy, and many other spas, are also resorted to by the subjects of cholelithiasis for the relief of their symptoms.

In England the waters of Bath may be taken with advantage to the patient.

*Salicylate of Soda* has been tried from time to time in the treatment of cholelithiasis with varying success. It has a distinct cholagogue action on dogs; and in Noël Paton's case of biliary fistula in a woman an increase of both the solid and watery constituents of the bile followed on the administration of the drug. Its employment in practice is advocated by several writers, and I have myself seen good results from its administration. It is well worth a trial, and may be given in doses of ten to fifteen grains three or four times daily. A draught of hot water after the administration of the drug will aid its action. The mild diaphoretic action which sodium salicylate not infrequently exerts will ease the patient even if the pain of the colic be not materially relieved by it.

*Salol* is recommended by some observers instead of salicylate of soda. Salicylic acid is excreted as such by the bile, and will therefore exert an antiseptic action in the biliary passages. It will not, however, dissolve a gall-stone.

*The Bile Salts.*—Glycocholate and taurocholate of soda have been tried in the treatment of cholelithiasis, but although they have a cholagogue action in dogs, practical experience does not show that they have

much effect on the course of the disease, and they are rarely used at the present time in England.

*Calomel* is recommended by a few physicians, and especially in cases in which the alkalies do not act well. It may be administered either alternately with the latter, or else by itself in repeated small doses. It must not be allowed to purge, and salivation must of course be avoided.

Duckworth\* recommends two grains of blue pill to be given every night for two or three weeks, then to be discontinued for a week or so, and again ordered for two or three weeks more. In this way the liver is kept well stimulated for some time, and the patients feel much better generally.

*Morphia* is essential in cases where the biliary colic is severe. It ought to be administered subcutaneously and in small doses ( $\frac{1}{6}$  of a grain) at first, as occasionally the subjects of biliary colic are very susceptible to its action. When the pain is very severe, morphia is often the only drug which at all relieves it. Persistent vomiting may at times call for its use.

*Belladonna*, in doses of one quarter of a grain of its extract, is frequently of much value in relaxing the muscular spasm which causes the biliary colic. It ought to be pushed until its physiological action on the pupil begins to appear. After its administration in combination with olive oil I have seen good results follow, and I have in my possession a biliary calculus which was passed *per anum* after such treatment.

\* 'Internat. Med. Clin.,' Series 4, vol. iv.

*Chloroform, Ether, and Turpentine*, either separately or in combination, have from time to time been recommended as being successful in the relief of pain in cholelithiasis. A combination of all three formed the much praised Durande's mixture, which was supposed to dissolve the calculi in the biliary passages. The relief of the symptoms which undoubtedly follows at times on the administration of these drugs is probably due to an antispasmodic action on the muscle-fibres of the biliary passages. They cannot possibly be excreted by the bile in quantity large enough to exert any solvent action on a calculus in the biliary passages.

*Use of Aperients.*—Care must be taken to see that the bowels act regularly every day, but without any purging. A daily dose of Carlsbad salts, or of a mixture of the sulphates of soda and magnesium and the phosphate of soda in equal parts, taken in a tumblerful of hot water before breakfast, acts very well in securing a satisfactory action of the bowels. They may, indirectly by sweeping out the contents of the intestines, and directly by the water in which they are taken, increase the flow of bile. At any rate they tend to prevent portal and hepatic congestion.

*Pilocarpine* is at times useful in removing the icteric tint from the skin and in relieving itching. It must be given in small doses of  $\frac{1}{8}$  to  $\frac{1}{6}$  of a grain once or twice a day, but as it tends to depress the heart its action must be carefully watched. In debilitated patients it should not be used at all.

*Olive Oil.*—The administration of oil to patients

suffering from attacks of gall-stones is a practice which dates back to the middle of the last century at least, and probably to an earlier period. At any rate, Coe,\* writing about 1750, recommends that oil of sweet almonds should be given in the disease, for "it is a soft lubricating thing which assists in relaxing the fibres of the passages and in easing the pain." He had seen good follow from the use of this form of treatment, but he does not seem to have ordered the oil in large doses.

In 1842 Dunglison† stated that biliary colic was often much relieved by the administration of large doses of olive oil, but he pointed out a source of deception by means of which the effect of the oil on the expulsion of biliary calculi may be greatly overestimated. He tells of a case of biliary colic which was treated by large doses of olive oil with good results, and in the stools passed by the patient after taking the oil were found numbers of concretions varying in size from a grape seed to that of a small pea. These, he pointed out, consisted of fatty matters, and were not gall-stones.

In 1880 Kennedy‡ again directed attention to the improvement which followed on the administration of large doses of olive oil in biliary colic, but he described the fatty concretions which were afterwards passed in quantity *per rectum* as gall-stones. Ball‡ pointed out the true nature of the concretions described by Kennedy, and since then other observers

\* Op. cit.

† 'Practice of Medicine.'

‡ 'Lancet,' Sept. 18th and 25th, 1880.

have fallen into the same error as Kennedy did, and have been corrected.

True gall-stones are, however, frequently passed by the bowel after this treatment, and I have an undoubted, flat, polyhedral, faceted, biliary concretion found in the stools of a patient who suffered from typical biliary colic which was treated by enemata of olive oil and by belladonna.

In 1892 Egasse\* published the results, as recorded in various journals, obtained by the treatment of fifty-four cases of biliary colic with large doses of oil. Recovery or improvement took place in 96 per cent. of the cases, and since this date cases have frequently been published in the medical journals in which relief of symptoms followed the adoption of the treatment. At the same time records of failures are also met with.

At best the treatment is an unpleasant one, but patients after suffering from biliary colic for a time will submit to it, and I have occasionally met with those who liked it, chiefly because of the relief which it brought to their sufferings.

When given by the mouth the unpleasant taste of the oil may be covered to some extent by adding a few grains of menthol and a tablespoonful of brandy to eight ounces of oil. Rosenberg added half an ounce of brandy, half a drachm of menthol, and the yolks of two eggs to about six ounces of olive oil. The whole of this mixture was to be taken in the course of four hours in several doses of one ounce each.

\* 'Bull. gén. de Thérap.,' Jan. 20th, 1892.

Some authorities insist on the patient lying over on the right side with the shoulders at a lower level than the pelvis, so that the expulsion of the oil from the stomach may be facilitated, and the tendency to nausea obviated.

The amount of the dose varies from five to twenty ounces *per diem*. Some patients stand the treatment much better than others. At times the oil cannot be retained in the stomach when first taken, and is vomited back at once, but after two or three repetitions of the vomiting the stomach seems to get used to the mass of fatty matter and retains it.

Much smaller doses of the oil—half to one ounce—repeated three or four times a day will often act as well, apparently, as the larger doses, and patients who cannot stand the latter will bear the smaller doses.

An enema of warm olive oil (ten ounces) repeated daily, will frequently relieve the symptoms as well as if the oil be given by the mouth. Such enemata are generally retained entirely, and part of the oil is absorbed into the circulation as fatty acid, soap, or as unchanged oil. I have seen this method of administering large quantities of olive oil give relief in several instances.

*Explanation of the Action of Olive Oil.*—Various theories have been advanced from time to time in explanation of the improvement of the symptoms of cholelithiasis which follows on the administration of olive oil, especially in large doses, in attacks of gallstones. Coe\* thought that oil acted well because it is a soft lubricating thing which assists in relaxing the

\* Op. cit.

fibres of the biliary passages, but how this happens he does not say.

Touatre\* was of the opinion that the oil entered from the duodenum through the ostium duodenale of the common bile-duct into the biliary passages. If this could happen, there is no doubt that the oil would dissolve any biliary concretions which it might meet with. It has also been suggested that the biliary passages would be lubricated in this way, and facilitate the passage through them of concretions. It is very improbable that oil can directly enter the biliary passages from the duodenum except under great pressure.

Virchow† has shown that the oil is absorbed from the alimentary tract and is excreted by the liver from the blood, and thus passes into the bile.

Other observers (Jankau‡) have proved by experiment that there is an increase in the amount of fat in the bile when that in the diet is increased.

Stewart§ considered that the oil is decomposed in the duodenum by the pancreatic juice into fatty acids and glycerine, and that the action of the latter on the duodenum is similar to its action on the rectum, namely, that it excites a powerful reflex peristalsis, which promotes the expulsion of bile and calculi from the biliary passages.

Rosenberg|| showed by experiment that the presence

\* 'Arch. roum de Méd. et Chir.,' 1887, vol. i, p. 99.

† 'Therapeut. Monats.,' 1890, p. 86.

‡ 'Arch. f. exp. Path. u. Pharm.,' Bd. xxxix.

§ 'Medical News,' Nov. 23rd, 1889.

|| Loc. cit.

of a large quantity of oil in the duodenum causes an increase in the amount of bile expelled from the biliary passages, probably by a reflex action, the extra quantity of bile being required to emulsify the extra amount of oil. Other observers (Prévost and Binet,\* etc.) were unable to confirm these results, but it is quite possible, or even probable, that Rosenberg's results are not altogether fallacious, for the supply of the digestive juices varies within certain limits with the demand for them.

A point which tells against the theories of Rosenberg, Touatre, and Stewart is that olive oil will frequently act as well in relieving biliary colic symptoms when given by enema as it does when given by the mouth. In my own opinion, the good results of the oil treatment are due to a combination of causes. In the first place it is quite possible that a good portion of the beneficial effects of large doses of olive oil, given *per os* or *per rectum*, can be attributed with some reason to the depressant effect which the introduction of such a quantity of fat into the system must have. By this depressant action, spasm of the muscle fibres in the wall of the bile-ducts, which causes pain or hinders the passage of a gall-stone, may be overcome with consequent relief to the symptoms. Large doses of olive oil will often act very beneficially in the spasmodic intestinal colic of plumbism, even after other remedies have failed (Weil† and Combemale‡). In the second place, not only is oil or fat absorbed into the blood from the intestinal tract, and excreted

\* Loc. cit.

† 'Lyon Médicale,' Dec., 1892.

‡ 'Bull. gén. de Thérap.,' cxxiv, p. 433.

by the liver cells, but a portion of the fatty acids and soaps formed by the changes which fat undergoes during digestion, and which are taken up by the portal capillaries, also passes through the liver cells into the bile. Oil, fatty acids, and sodium or potassium soaps are all good solvents of cholesterin, and will act readily on this substance, even when they are present in small quantity in suspension or solution in a fluid (bile in this instance) which comes in contact with it in the crystalline form or in a gall-stone. Soap especially, in weak solutions ( $\cdot 1$  to  $\cdot 5$  per cent.), has a strong solvent action on gall-stones containing cholesterin. Thus I found that a gall-stone placed in a  $\cdot 5$  per cent. solution of *sapo animalis* in distilled water, and kept at the body heat in an incubator, lost 34 per cent. of its original weight in three weeks, and a similar concretion in a  $\cdot 1$  per cent. solution lost 14 per cent. of its weight in the same time.\*

Hoppe-Seyler,† from analysis of five samples of human bile taken *post-mortem* from the gall-bladder, found "soaps" present in them to the average extent of 1.39 parts in 100. The amount of fats was  $\cdot 73$  in the same quantity of bile. From this observation of Hoppe-Seyler's and from my own work it will be seen that soap may be present in solution in the bile in quite sufficient quantity to exert a strong solvent action on gall-stones—at any rate on those containing cholesterin. *Sapo animalis* and *sapo durus* are, in fact, the only drugs which can pass by the natural processes of digestion and absorption into the bile in

\* 'Manch. Med. Chron.,' Dec., 1893.

† Ref. Gamgee, *op. cit.*, p. 346.

sufficient quantity to exert any solvent action on a gall-stone in the biliary passages.

Finally, I think it is very probable, as Rosenberg suggests, that a large amount of oil in the duodenum sets up a reflex expulsion of bile from the biliary passages, which may wash out a small, obstructing concretion through the ostium duodenale, or at any rate create a demand for the formation of more bile, and thus prevent the tendency to biliary stagnation.

*Soap* (*Sapo durus* or *Sapo animalis*) has been given in the form of pills in 5 to 10 grain doses three times a day, and continued for some time with apparently a beneficial effect on the course of the disease. It tends to prevent relapses.

*Glycerine* in doses of one to two tablespoonfuls has been recommended by Ferrand\* as being useful in cutting short attacks of biliary colic, and when given in smaller doses every day in preventing relapses.

### Hygienic Treatment of Cholelithiasis.

*Exercise.*—The movements of the body generally, and especially of the abdominal muscles, aid in the expulsion of bile from the biliary passages and gall-bladder, and tend to prevent its stagnation. It is, therefore, an important factor in the treatment of cholelithiasis. Exercise on horseback is suitable for such patients as are able to ride and can afford to do so. Rowing also brings into action the muscles of the abdomen to a very great extent, but there are not many subjects of gall-stones who can indulge

\* 'Bull. Méd.,' 1892.

in this form of exercise. In the more active patients tennis and golf are of much value.

Duckworth\* advises that when a patient is liable to frequent attacks of biliary colic, exercise should not be indulged in when food is passing from the stomach into the duodenum—namely, about an hour and a half after a meal. The biliary passages are then in an active expulsive condition, and exercise might easily dislodge a calculus.

When the patients are unable to get about out of doors much, the system of home gymnastics, especially with the movements of the body, which has been introduced of recent years, will, if regularly carried out, tend to prevent biliary stagnation, and the more active patients who feel inclined to try the model horse or model rowing-machine in their own homes will probably derive benefit from its use.

In the intervals between the attacks, and when all acute symptoms and distension of the gall-bladder have subsided, gentle abdominal massage, performed three or four times a day over the right hypochondriac region, is of use in aiding the expulsion of bile from the gall-bladder and ducts. This ought not, however, to be undertaken during the acute stage or if the gall-bladder be distended, for fear of rupturing the wall of the biliary passages. Any clothes, corsets especially, which encircle the body too tightly, preventing its free movements and hindering the action of the diaphragm, must be forbidden.

*Baths* are useful sometimes in the treatment of the

\* 'Internat. Med. Clinic.,' Series 4, vol. iv.

disease. When practicable, a bath as hot as the patient can bear it will often relieve the pain, and hot poultices or fomentations over the region of the gall-bladder and the pit of the stomach are at times very soothing.

A cold, tepid, or warm bath taken daily is a simple measure which tends to keep up the general bodily health, and which may be recommended with advantage to the subjects of gall-stones.

### **The Dietetic Treatment of Cholelithiasis.**

The diet taken by subjects of cholelithiasis must be carefully attended to. Various opinions are held as to the nature of the different articles of food which ought to be ordered; but there is a general consensus of opinion on one point, namely, that foods and alcohol which derange the liver must be forbidden. Fat should not be taken if there be much jaundice present with clay-coloured stools, as bile seems to be essential for its proper digestion.

In a former chapter I endeavoured to show that the bile salts which help to dissolve the cholesterin are derived from nitrogenous foods, and are diminished in amount when such foods are not taken.

Basing my conclusions on this "theory," I consider that the lighter forms of nitrogenous foods ought to form an important portion of the diet of the subjects of cholelithiasis, and that women especially should be advised not to live too much on carbohydrates, fats and sweets. Entrées, though containing a good proportion of nitrogenous foods, are

unsuitable, as they frequently cause biliary derangements. The heavy, butcher's meats are not advisable for the old people who are so often affected with the disease, or for gouty subjects. In addition to the lighter nitrogenous foods, the subjects of gall-stones should take a fair amount of fat in the form of fresh butter, cream, or oil in salads, if they can do so without any discomfort, to increase the quantity of fats and soaps in the bile, both of which are good solvents of cholesterin.

Alcohol must, from its tendency to affect the liver, be limited to a glass or two of the lighter wines, or an ounce or so of good whisky with the dinner. Too much tea must also be avoided.

### **Medical Treatment of Intestinal Obstruction from Gall-stones.**

Very little can be done medically for intestinal obstruction from gall-stones beyond keeping the patient at rest and treating any symptoms which call for attention. Nature will often succeed in causing the expulsion of the obstructing body from the bowel.

Belladonna given in large doses until its physiological action on the body becomes apparent, may aid in the expulsion of the gall-stone. It may be used internally, or be applied externally over the abdomen in the form of a fomentation. It acts by relaxing the muscular spasm which plays an important part in preventing the passage of the obstructing calculus.

Opium is also of much value for the same reasons ; but any drugs which increase intestinal peristalsis do more harm than good.

Enemata of olive oil or of warm water introduced carefully through a long tube can do no harm, and may do good in certain cases.

## CHAPTER XIV.

The Surgical Treatment of Cholelithiasis—Indications for Surgical Aid in the Treatment of Calculous Affections of the Biliary Passages—Views of Different Authorities in England and on the Continent on the Subject—The Surgical Treatment of Intestinal Obstruction from Gall-stones.

**Indications for Surgical Aid in the Treatment of Calculous Affections of the Biliary Passages.**

MANY authorities hold different opinions as to when surgical measures must be adopted for the relief of cholelithiasis and its complications. As this is an important matter, it will be advisable to give rather fully the views recently expressed by some of the observers who have had much experience in the treatment of the disease.

**In England.**

In Mayo Robson's\* opinion the following conditions seem to be indications for operative treatment in cholelithiasis :

- (1) Frequently recurring biliary colic without jaundice, with or without enlargement of the gall-bladder.
- (2) Enlargement of the gall-bladder without jaundice, even if unaccompanied by great pain.
- (3) Persistent jaundice ushered in by pain, and

\* ' Brit. Med. Journ.,' April 28th, 1894.

where recurring pains, with or without ague-like paroxysms, render it probable that the cause is a gall-stone in the common duct.

(4) Empyema of the gall-bladder.

(5) Peritonitis starting in the right hypochondrium.

(6) Abscess around the gall-bladder or bile-ducts, whether in the liver, or under, or over it.

(7) Some cases where, although the gall-stones may have passed, adhesions remain and prove a source of pain and illness.

(8) A mucous or biliary fistula.

(9) Certain cases of jaundice with distended gall-bladder dependent on some obstruction in the common duct; but in such cases the increased risk must be borne in mind, as malignant disease will probably be the cause of the obstruction.

In cases of protracted jaundice, where there is a suspicion of the presence of a hæmorrhagic diathesis, Mayo Robson administers calcium chloride in large doses with a view to increase the coagulability of the blood, and to prevent hæmorrhage after operation. He gives 15 grains of the drug every four hours for two days previous to the operation.

Greig Smith\* is of the opinion that persistent obstructive jaundice indicates, and at the same time contra-indicates, operation.

Jacobson, in his work on 'The Operations of Surgery' (1891), quotes this opinion of Smith's, and presumably agrees with it.

Other surgeons, however, consider that long-con-

\* 'Abdominal Surgery,' 1891.

tinned and severe jaundice does not necessarily put the blood into such a condition as to cause uncontrollable hæmorrhage, and that it is not in itself always a contra-indication for operation. Each case must be judged on its individual merits, as Naunyn advises, for many patients with marked and prolonged jaundice will in all probability die unless operative treatment be adopted. In the majority of cases no bad results which can be attributed to the cachexia of jaundice arise from operation.

### Opinions of Continental Surgeons.

The indications for operative treatment for cholelithiasis, which are generally recommended in Germany, as stated by Gumprecht,\* are as follows.

Colic or other severe symptoms, which get worse in spite of medical and hygienic treatment; obstruction of the common duct which has persisted for some months; the threatened onset of cholæmia and pyæmia; biliary fistulæ without free escape of their discharge; adhesions of the gall-bladder with severe symptoms; rupture of the gall-bladder and threatening peritonitis; and finally, all conditions which justify an exploratory laparotomy.

Continental authorities are, however, divided into two schools,—one which teaches early operation, and the other late surgical interference. The supporters of the early operation maintain that the prognosis is much better if the case be dealt with before the patient has been debilitated by long duration of the symptoms. Riedel defends this procedure by the

\* 'Deutsch. med. Woch.,' 1895, No. 20.

following arguments :—No stone above  $\frac{3}{4}$  cm. ( $\frac{3}{8}$  inch) in diameter can pass *per vias naturales* from the biliary passages to the alimentary tract, and all above this size call for surgical interference. According to Courvoisier, 34 per cent. of all biliary calculi are equal to, or greater than, a hazel-nut in size, and therefore about one third of all cases of cholelithiasis are suitable for surgical treatment. If cholagogues be administered to such patients, and the stone pass into the biliary passages, an operation for its removal is much more severe than a simple operation on the gall-bladder. Colic without jaundice is therefore an indication for operation, as it means that the stone remains in the gall-bladder, and is too great to emigrate spontaneously. When there is a suspicion that hydrops cystidis felleæ is present, and that the stone still sticks in the neck of the bladder, operation is called for. Medical treatment only, is indicated if the colic come on without previous protracted premonitory symptoms, and if the jaundice follow rapidly, for when premonitory symptoms are absent it may be assumed that the jaundice is caused by a stone passing along the common duct.

Some of the patients with small calculi (Courvoisier's 66 per cent.) may also have to be helped surgically.

Winiwater considers that in all cases in which a biliary calculus reveals its presence by symptoms, surgical aid is indicated.

The advocates of later operation consider that surgical treatment should only be adopted in acute infectious cholecystitis; chronic empyema of the

gall-bladder; pericholecystitis, which is indicated by persistent sensitiveness and enlargement of the gall-bladder, and which points to suppuration of the contents of the latter; persistence of retention-swellings of the gall-bladder after the cessation of the attacks of colic. In the latter condition there is probably a large concretion present, which may cause further and severer complications. The onset of these severer complications is uncertain, and as operative help may, if delayed too long, be of no use, it is advisable as a rule to treat simple retention-swellings of the gall-bladder, especially in the labouring classes, surgically.

*Naunyn's*\* views on the subject of the operative treatment of cholelithiasis are as follows :

(1) Operation is absolutely necessary in the early stages of biliary colic, if rupture of the biliary passages has taken place and general peritonitis is threatening, and in cases of acute infectious cholecystitis. The prognosis in both these classes of operation is fair if undertaken in time.

(2) In cases of chronic empyema, where there is no probability of spontaneous recovery, and where there is a danger of general infection, perforation, and the formation of fistulæ, operation is advisable, provided that jaundice be absent. The prognosis of operations on cases in which a distinct tumour of the gall-bladder can be felt, and in which there is no jaundice, is good (mortality 6 per cent.).

(3) The prognosis of operations on simple distensions of the gall-bladder is good enough to recommend surgical treatment for this condition, especially

\* *Op. cit.*, p. 170.

when other severe symptoms of cholelithiasis are present.

(4) Great care must be observed in recommending operation in cases where jaundice has been present for some time, for such patients are anæmic, and often not capable of undergoing the shock of operation. Chronic jaundice also tends to cause hæmorrhage from very trifling causes. Of seventy cases with jaundice which were operated upon, thirty-four died (48·7 per cent.). It must further be remembered that in cases where jaundice is present and has been so for some time, there are very likely to be complications—carcinoma of the bile-ducts or pancreas, severe pericholangitis or pericholecystitis, which of themselves add to the dangers of operation. There are, however, some cases of chronic jaundice, accompanied by other severe symptoms, which would die certainly unless operated upon, and which may be saved by surgical interference.

It must be left to the operator to decide in each case whether or not it is advisable to interfere surgically.

*Courvoisier*\* only undertakes operative treatment under the following conditions.

(a) When the symptoms have lasted for some time and are getting worse, and which, in spite of medical treatment, are unbearable, confine the patient to bed and render him unfit for work.

(b) When the symptoms are of shorter duration, but their cause evidently cannot be removed by internal treatment (persistent obstruction of the common duct,

\* Op. cit., p. 321.

hydrops, empyema, fistulæ, and carcinoma of the gall-bladder).

(c) When the symptoms have existed for a short time only, but, if allowed to continue, will cause danger to life (injuries to, or ulcerative perforation of the biliary passages).

In cases of jaundice from protracted obstruction of the common bile-duct where there is a possibility of the blood being in a poor condition, the surgeon must examine carefully the skin, mucous membranes, and excretions of the patient for evidence of a hæmorrhagic diathesis, and if such be present he must only undertake an operation when absolutely obliged.

### The Surgical Treatment of Intestinal Obstruction from Gall-stones.

The question of the advisability of operating for this condition is still *sub judice*. Hutchinson\* finds that the mortality of cases operated on is a little over 50 per cent., whilst Courvoisier† states that in cases treated medically throughout it is 44 per cent. The surgical mortality has been decreasing greatly during recent years, and in the hands of men who are skilled in abdominal surgery, laparotomy for intestinal obstruction from gall-stones affords a better prognosis than statistics collected from all sources would lead one to believe.

The true cause of an intestinal obstruction cannot always be made out until the abdomen has been opened, and therefore the surgeon is often obliged to

\* 'Brit. Med. Journ.,' 1895, i, p. 195.

† Ref. Naunyn, op. cit., p. 149.

operate for the relief of the obstruction when he might not do so by choice were he certain that the symptoms arose from the impaction of a gall-stone in the intestine.

The patient has a much better chance of benefiting by surgical treatment if the operation be undertaken before great debility has time to develop. The more severe the patient's condition, the more dangerous does laparatomy become.

## CHAPTER XV.

The Various Operations on the Gall-bladder in Cholelithiasis—Puncture of the Gall-bladder—Cholecystostomy—Cystopexy—Ideal Cholecystotomy or Cholecystendysis—Cholecystenterostomy—Cholecystectomy—Operations on the Biliary Passages in Cholelithiasis—Sounding or Catheterisation—Extraction of Biliary Calculi from the Ducts, Cholelithotomy, Choledochotomy, Choledocholithectomy, and Choledochoduodenostomy—Choice of Operation—Surgical Treatment of Intestinal Obstruction from Gall-stones.

### Operations on the Gall-bladder in Cholelithiasis.

1. Puncture of the Gall-bladder.—Puncture of the gall-bladder through the abdominal wall with an exploring needle is occasionally done as a means of diagnosis, but it is not without serious dangers, as mentioned in a former chapter. Even when a fine needle is used the contents of a distended gall-bladder may easily, and often do, escape through the puncture in its wall, and if the fluid which exudes be septic in character a local peritonitis which may cause much trouble, or even a fatal general peritonitis, will ensue. The case published by Williams\* (of distended gall-bladder due to cancer of the duodenum) is an instance of general peritonitis arising from this cause and terminating eventually in the patient's death.

The emptying of a distended gall-bladder by

\* Brit. Med. Journ., January 25th, 1896.

aspiration through the abdominal wall is a procedure which ought not to be adopted for the same reasons, except under very exceptional circumstances. Murphy\* cannot recommend it, and states that 25 per cent. of the cases treated in this way end fatally.

An exploratory laparotomy developing into any operation necessary for the relief of the condition found is a much better and safer course to adopt.

**2. Cholecystostomy or Cholecystotomy.**—Cholecystostomy, or cholecystotomy as it is sometimes called, consists in the formation of a biliary-cutaneous fistula by incising the gall-bladder and stitching the edges of the wound to those of the abdominal incision.

There are two methods of performing the operation, both of which are frequently adopted.

(A) The operation may be done in *two stages*. In the first the unopened gall-bladder is drawn up into the abdominal wound, and fixed there by sutures passed through its walls which bring the peritoneum covering it into apposition with that lining the inner surface of the abdominal wall. The case is then left in this condition for two or three days, when, the two surfaces of peritoneum in contact having adhered and closed up the abdominal cavity, an incision is made through that portion of the gall-bladder which presents through the abdominal wound, and its contents evacuated. By this operation the escape of any infectious fluid into the peritoneal cavity is avoided, but such an event ought not to happen if the next operation (B) be done with ordinary care.

From the records of thirty-one cases operated

\* 'Brit. Med. Journ.,' 1894, i Elitome, p. 49.

on previous to 1890, Courvoisier\* found that sixteen patients were cured, ten were left with a biliary or mucous fistula, one was improved, and four died from malignant disease. Murphy† and Martig‡ (1893) both state the mortality to be 10 per cent.

(B) The whole of the operation may be completed in *one stage*, in which the gall-bladder is opened and fixed to the abdominal wall. There are two ways of performing this operation.

(a) The gall-bladder is emptied before it is stitched to the edges of the abdominal wound (natural cholecystostomy of Lawson Tait). The mortality in this variety of operation was, up to 1890, 22 in 104 cases (Courvoisier). In 17 of the cases a fistulous opening remained, and the rest were cured or materially relieved (mortality 1893, 17 per cent.—Martig).

As a further modification of this operation the cystic duct may be ligatured to avoid the formation of a fistula.

(b) The gall-bladder is first fixed to the abdominal wall and then opened.

The statistics of this variety of operation are not satisfactory, as eight out of fourteen cases were in more or less of a cholæmic condition at the time of operation, and died. Fistulæ remained in three patients, and the remaining three recovered (Courvoisier, 1890).

Murphy (1893) states the mortality of cholecystostomy in one stage to be 19 per cent.

\* Op. cit.

† Loc. cit.

‡ Ref Gumprecht, 'Deutsch. med. Woch.,' 1895, No. 20.

Up to the beginning of 1894 Mayo Robson\* had performed cholecystostomy in fifty-five cases of cholelithiasis, uncomplicated by malignant disease, without a death. A fistula remained in three of these cases only, one of which was afterwards cured by excision of the gall-bladder (cholecystectomy), and the others by cholecystenterostomy. The fifty-two remaining cases all did well.

This operator prefers to complete the operation in one stage, and he always sutures the edges of the incision in the wall of the gall-bladder to the aponeurosis, and not to the skin, of the abdominal wall. A drainage-tube is introduced into the gall-bladder for a few days, when it is removed, and the biliary-cutaneous fistula allowed to close naturally.

Martig states that a permanent fistula discharging mucus or a purulent fluid results in 20 per cent. of the cases of cholecystostomy—at any rate, in the “one stage” operation. Mayo Robson’s splendid results do not bear out this statement.

**3. Cholecystopexy.**—This operation is not often performed. It consists in the incision of the gall-bladder, suture of the edges of the wound to the abdominal wall, and closure of the incision by extra-peritoneal suture after the contents of the gall-bladder have been removed. It is stated that biliary-cutaneous fistulæ are avoided by its adoption, but a great objection to the operation is that the surgeon can never be sure that he has been able to remove all the obstructing concretions from the biliary

\* ‘Brit. Med. Journ.,’ April 28th, 1894.

passages and gall-bladder, and relapses are very liable to occur if the gall-bladder be closed at the end of the first operation. Up to 1890 one patient out of four operated on died (Courvoisier), but since this date the mortality has decreased to 10 per cent. (Martig).

4. "Ideal" Cholecystotomy, or Cholecystendysis.—Ideal cholecystotomy is more often undertaken than the previous operation. In it the gall-bladder is opened, emptied of its contents, closed up again, and replaced in the abdominal cavity at the same operation.

This operation is practised by many surgeons on the Continent, and its advocates state that its advantages are that it is quick and safe, the gall-bladder is preserved, recovery from it is rapid, adhesions of, and traction on the gall-bladder, biliary-cutaneous fistulæ, and weakness of the abdominal wall are avoided. It can only be carried out in cases in which the gall-bladder is sufficiently free from adhesions, and the common duct is patent and free from calculi. Empyema and atrophy of the walls of the gall-bladder are contra-indications to its adoption.

The great objection to this, as to the previous form of operation, is that it is impossible to tell when all the calculi have been removed from the biliary passages, and relapses are very liable to occur. It is a very common occurrence to meet with cases in which many calculi escape through a biliary-cutaneous fistula after all that could be felt were removed from the gall-bladder and bile-ducts at the time of operation.

Murphy collected from literature the records of thirty-five cases with eight deaths.

According to Martig, the mortality from the operation amounts to one in seventeen on all cases recorded, and in recent times, in the hands of certain special operators, it has been reduced to 0 per cent.

**5. Cholecystenterostomy** is the artificial formation of a gall-bladder-intestinal fistula. This result is obtained by making an incision through the wall of the gall-bladder—generally at the fundus—and one through the wall of a conveniently-situated portion of the intestine, and then uniting the two organs by fixing the edges of the incisions in them to each other by means of sutures or “intestinal anastomosis buttons,” leaving a false passage between the cavities of the two organs.

This rather difficult and somewhat complicated operation is often performed at the present time, some surgeons being especially fond of it. In the hands of its advocates it has usually been successful.

According to Murphy,\* the mortality in this operation was up to 1893, 36 per cent. when the union was made by suture, but when made by his intestinal anastomosis button only one out of thirty-nine cases of non-malignant obstructive jaundice died.

Cholecystenterostomy should be performed where there is obstruction in the common duct from an impacted gall-stone which cannot be removed or relieved by simpler surgical measures. Murphy† is a great advocate of this form of operation, and considers

\* ‘Lancet,’ April 27th, 1895.

† ‘Brit. Med. Journ.,’ Epit., 1894, p. 49.

that it is indicated in all cases where it is desirable to drain the gall-bladder from accumulations therein ; in all cases of perforation of the common duct into the abdominal cavity where the duct must be obliterated by the reparative process ; in all cases of cholelithiasis when obstruction of the common duct is present, or where the reflex disturbances of digestion are marked ; in all cases of cholecystitis, either with or without gall-stones, and in all profusely discharging fistulæ. It is contra-indicated where the gall-bladder is very small, and where the bowel is too closely fixed by adhesions to be brought into contact with the gall-bladder. If the common duct be occluded, the gall-bladder should be amputated just above its neck, leaving a sufficient portion to be approximated to the duodenum in the usual way. Murphy uses his button in all cases of cholecyst-enterostomy.

Elliot,\* on the other hand, considers that this operation is undertaken too readily in the relief of gall-stones, and that incision of the ducts (q. v.) or of the gall-bladder, followed by immediate suture after the removal of the stone, is the proper operation, especially in recent cases.

**6. Cholecystectomy** is the extirpation, by excision, of the gall-bladder. The cystic duct is ligatured, the gall-bladder dissected away from its attachments, and then cut off close to the ligature.

It is a favourite operation with some Continental surgeons. Up to 1890 Courvoisier found that out of

\* 'Annals of Surgery,' July, 1895.

forty-seven cases ten had died directly, and two indirectly from the operation. Murphy's statement of the mortality is 17 per cent. up to 1893.

Cholecystectomy is indicated when, after cholecystostomy, there is a persistent biliary-cutaneous fistula, with a mucous or purulent discharge, and when the cystic duct is obliterated; where under similar circumstances, owing to accumulation of fluid in the gall-bladder, the pain recurs as soon as the fistula has closed (Robson); in hydrops and empyema of the gall-bladder when it is already disconnected from the common duct by occlusion of the cystic duct; in severe diseases of the wall of the gall-bladder,—ulceration, gangrene, contraction, &c.; in severe chronic "cholelithiasis vesicularis"; in internal rupture of the gall-bladder when suture is impossible (Murphy). It is contra-indicated by strong adhesions of the gall-bladder and its close attachment to the liver, and in all permanent closures of the common duct (Murphy) and when it is uncertain if all the concretions have been removed from the gall-bladder and large ducts.

The removal of the gall-bladder does not of necessity prevent the repetition of attacks of biliary obstruction and colic, for calculi may form *de novo* in the bile-ducts.

### Extraction of Biliary Calculi from the Bile-ducts.

1. **Cholelithotrity, Cholelithotripsy.**—Biliary calculi can at times, during operations on the gall-bladder, be removed from the cystic duct by the finger introduced into the former, but only when they are situated low down in the duct near the neck of the

gall-bladder. They may also, when soft, be broken down by the finger-nail and extracted piecemeal from the same situation. But when they lie higher up in the cystic duct, and near its junction with the hepatic duct, this procedure is impossible, unless the duct be widely dilated.

It is also sometimes possible to work a concretion down towards the gall-bladder from the large ducts, especially from the cystic duct, by manipulating it with the fingers working outside the wall of the duct. In dilated ducts this may be effected successfully, but when the ducts are of practically normal calibre it is very difficult to move concretions in them. Attempts to extract calculi from the cystic duct by means of forceps introduced through the incised gall-bladder are not advisable, for unless the stone can be steadied by grasping it with the fingers through the wall of the duct, it may easily be pushed on into the hepatic or common duct by the forceps. Stones in the latter situations are more difficult to remove than those in the cystic duct.

If concretions in the large extra-hepatic ducts cannot be removed by any of the above simple methods, attempts may be made to crush them where they lie. This may be done either by means of the fingers and thumb or by padded forceps. In either method the concretion is seized by grasping it through the wall of the duct from the peritoneal cavity.

The use of the fingers is much more preferable to that of forceps, for the pressure applied can be estimated more accurately by them, and injury to

the wall of the duct is less likely to result than if forceps be used. When the concretions are soft or very friable, good results may follow from this method of treatment, and many cases have been recorded in which biliary calculi were easily broken up by the fingers. The remains of the calculi are left to come away by themselves, generally through a biliary-cutaneous fistula.

The *needling* of calculi in the biliary passages is recommended by some surgeons. The needle is passed through the wall of the duct, and the concretion broken up with it. Teale\* has recorded the results of three cases treated in this manner. Two were successful, but the third case died with symptoms of "severe abdominal pain." Teale attributed the death of this patient "to the difficulty of the manipulations caused by the stony hardness of the calculus."

Knowsley Thornton† has successfully treated several cases in which a gall-stone was lodged in the common duct by needling and crushing, and thinks such a procedure is worthy of more attention than it has hitherto received.

**2. Choledocholithectomy, Choledochotomy.**—Biliary calculi are perhaps best removed from the cystic, hepatic, and common ducts through an incision in the wall of the duct followed by immediate suture of the wound. The operation is called that of *choledocholithectomy* or *choledochotomy*, although these terms are

\* 'Brit. Med. Journ.,' Feb. 2nd, 1895.

† Ibid., Feb. 29th, 1896.

usually applied more definitely to the excision of calculi from the common duct (ductus choledochus). Elliot\* considers that this operation ought to be adopted in the majority of cases of obstruction of the extra-hepatic ducts by calculi, especially when the illness is of recent origin. The gall-bladder need not of necessity be opened during this operation unless it contain calculi. By the adoption of cholelithectomy more frequently in chosen cases than is customary at the present time, the severer operations of cholecystotomy or cholecystenterostomy may often be avoided. The excision of calculi from the common duct is facilitated by the dilation which this passage undergoes behind, and as a result of, the impaction of a calculus in it.

Some surgeons prefer to do a cholecystotomy as well as cholelithectomy for drainage purposes. Thus Kehrl† removed calculi in the cystic duct through an incision in its wall in seven cases. The wound was immediately sutured, and cholecystotomy was performed for draining the cystic duct and to prevent straining of the sutures by pressure from the bile. The cases all did well.

Stones in the hepatic and common bile-ducts may be treated in the above manner if they cannot be easily crushed between the thumb and finger or be manipulated by them into the duodenum or back into the gall-bladder. Needling, or crushing with padded forceps, may seriously injure the duct without the operator being aware of it, and should only be under-

\* 'Annals of Surgery,' July, 1895.

† Deut. Zeitsch. f. Chir., 1894.

taken if the duct cannot be raised to allow of the proper introduction of sutures.

Terrier\* collected twenty cases of removal of calculi through incisions in the wall of the common duct. Of these five died—one from shock and one from leakage of the bile, the others from causes not attributable to the operation. He thinks that choledochotomy is the operation indicated when calculi are in the common bile-duct. Cholecystotomy ought to be done subsequently to the suturing of the wound in the duct where, from pathological conditions, drainage of the duct is advisable, or where the sutures have not been put in very well, and pressure on them must be avoided (Elliot†).

Fenger‡ performed choledochotomy on five cases of calculi in the common duct, with four recoveries. He considers that other operative procedures are rarely necessary in such cases.

Quénu§ suggests that when the common duct cannot be reached to enable sutures to be put in after the excision of a calculus, the wound in its wall should be allowed to heal by granulation. To allow of this the common duct must be patent. He carried out this method with success in one case. A drainage tube must be left in the abdomen to allow the bile which is extravasated to escape. He states that the wound heals quickly and spontaneously, and that the drainage-tube need only be left in for a day or two.

\* 'Rev. de Chir.,' Nov. 12th, 1892.

† Loc. cit.

‡ 'Brit. Med. Journ.,' 1896, Epit., p. 54.

§ 'Prog. Méd.,' 1895, p. 289.

3. **Choledochoduodenostomy.**—Kocher,\* in operating on one case for a complete obstruction of the common bile-duct, found the impacted calculus lodged in it behind the duodenum. He could not separate the two structures sufficiently to enable him to do an ordinary choledochotomy, so he opened the duodenum by means of an incision in its anterior wall, and then cut through its posterior wall from the lumen of the organ down on to the stone in the common duct, which he could then easily remove. The edges of the incisions in the posterior wall of the duodenum and in the wall of the common duct were then sutured to each other so as to form a biliary-duodenal fistula. The case made a good recovery.

The operation of making a fistulous passage between the common bile-duct and the duodenum is only carried out in very exceptional cases when no other procedure can be adopted. The above case of Kocher's is an example in point, but the operation is generally done by only one incision into the duodenum, namely into that portion lying nearest to the common duct. The edges of this incision are then stitched to the opening in the wall of the common duct, as in Kocher's case. The operation is very difficult to perform owing to the depth of the structures involved in it.

### Choice of Operation.

Cholecystostomy and "ideal" cholecystotomy (cholecystendysis) are generally looked upon by English and other surgeons as the most preferable operations in cases of cholelithiasis. Some surgeons

\* 'Korresp. für Schw. Aerzte,' 1895, No. 7.

prefer the immediate suture of the wound in the gall-bladder and the replacing of the latter in the abdominal cavity, whilst others create a temporary biliary fistula. Both methods yield good results in the hands of their various advocates.

Cholecystectomy is reserved for cases in which the above operations are insufficient, and Knowsley Thornton\* looks upon cholecystenterostomy as a valuable aid to surgical failure rather than an advance in surgery. It is, however, the only resource in incurable obstruction of the common duct. If, after opening the gall-bladder, it be found impossible to clear the ducts of calculi, the operations of cholelithotrixy or choledochotomy must be undertaken, or the case may be left with a fistulous opening through which stones may escape by themselves in the course of a few days. The escape of the calculi may, in certain favourable cases, be aided by the daily injection of warm olive oil, oleic acid, or a .25 per cent. solution of *sapo animalis* in distilled water through the fistulous opening into the biliary passages. This procedure is very simple and free from danger if it be carried out as described by the writer.† The oil reaches the concretion in the cystic or common ducts without any difficulty, and it will quickly cause a diminution in their size by dissolving the parts with which it comes in contact.

Mayo Robson prefers cholelithotrixy, which he has successfully performed on numerous occasions by means of his finger and thumb, to the more formid-

\* Loc. cit.

† 'Brit. Med. Journ.,' April 20th, 1895.

able procedure of incising the ducts or fixing the gall-bladder to the intestine. He considers that choledochotomy with immediate suture of the duct is not an easy matter, on account of the depth of the parts to be coapted.

Murphy\* cannot recommend cholelithotripsy on account of the danger of injuring the walls of the duct whilst crushing the stone, so as subsequently to cause a perforation. He is of opinion that choledochotomy with subsequent suture of the duct should be undertaken when the stone is large and firmly impacted in the common duct, especially when the cystic duct is obliterated, and the formation of a gall-bladder-intestinal fistula is impracticable, and when there is ulcerative perforation of the wall of the duct, and the tissues are in a healthy condition. If the tissues be otherwise the duct should be excised at this point, both ends tied, and cholecystenterostomy performed.

The mortality in all the above operations on the gall-bladder and biliary passages in cases of cholelithiasis has decreased greatly during the last three or four years, and when calculated from the results obtained by surgeons who pay special attention to the disease, is far less than an examination of all the recorded cases would show.

### Surgical Treatment of Intestinal Obstruction from Gall-stones.

The obstruction from a gall-stone may be overcome after opening the abdomen, by breaking the stone *in situ* with a needle passed through the wall

\* Loc. cit.

of the intestine, by working the stone on through the bowel and ileo-cæcal valve or by opening the intestine and removing it.

Many surgeons (Mayo Robson,\* Barker,\* &c.) condemn the needling of an impacted gall-stone through the intestinal wall which is already damaged by the stone as dangerous.

In a few favourable cases where operative treatment has been undertaken within a short time after the onset of obstructive symptoms, and the obstructing calculus is not too large and is near the lower end of the ileum, it may be pushed on through the ileo-cæcal valve into the colon. Such cases are, however, very rare, for generally the calculus is found to be somewhat adherent to the intestinal wall, and the latter is in too inflamed a condition to allow of the manipulation of the stone through it. The bowel below the obstruction is contracted, but above it is dilated with flatus, &c. The surgeon then, as a rule, has no choice in the matter, but is obliged to remove the calculus through an incision in the intestinal wall. If possible, it is better to move the stone upwards through the dilated intestine—a procedure which may at times be accomplished when a downward movement is impossible—until a portion of the intestine is reached which is in a less inflamed condition than that at the seat of impaction, and remove the calculus there.

\* 'Brit. Med. Journ.,' 1895, i, p. 195.



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